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REPORT OF PROFESSOR DAVID M. CUTLER

IN RE: NATIONAL PRESCRIPTION OPIATE LITIGATION, CASE NO. 1:17-MD-2804

CASE TRACK 3, LAKE AND TRUMBULL COUNTIES

APRIL 16, 2021

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I. Introduction

1. My name is David Cutler. I am the Otto Eckstein Professor of Applied Economics at Harvard University. I have appointments in the Department of Economics, the Harvard Kennedy School, and the Harvard T.H. Chan School of Public Health. I have been on the faculty at Harvard for over 25 years. I received a Ph.D. in Economics from the Massachusetts Institute of Technology in 1991 and an A.B. from Harvard University in 1987.

2. I specialize in Health Economics and Public Economics. I have published more than 200 articles and have written two books on the economics of health care. I am a former editor of the Journal of Health Economics and a former Associate Editor of the Journal of Economic Perspectives, the Journal of Public Economics, and the World Health Organization Bulletin.

3. I have won a variety of awards for my scholarship including the Griliches Prize in 1999, the Ken Arrow Award from the International Health Economics Association for best paper in health economics in 2000, the Eugene Garfield Award from Research!America in 2003, the David Kershaw Prize from the Association for Public Policy and Management in 2004, the Biennial award for distinguished contribution to the literature in population from the Section on the Sociology of Population of the American Sociological Association in 2006, the John P. McGovern Award from the Association of Academic Health Centers in 2009, the Distinguished Leadership Award from the Center for Connected Health in 2011, the MetLife Silver Scholar Award from the Alliance for Aging Research in 2011, and the Carpenter Award from Babson College in 2018. I was co-recipient of the American Society of Health Economists (ASHEcon) award for best health economist in the nation age 40 and under in 2006. I am currently the president-elect of ASHEcon and will be the president next year. I am a member of the

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American Academy of Arts and Sciences and the National Academy of Medicine. I was named one of the “30 for the Future” by Modern Healthcare magazine in 2006 and one of the “50 most influential men under age 45” by Details magazine in 2007. An article in 2012 listed me as the health economist with the highest h-index in the world.¹ The h-index is a widely used measure of scholarly productivity and citation frequency.

4. In addition to my scholarly activities, I have a record of service in the public sector. I served jointly on the Council of Economic Advisors and National Economic Council in 1993, with primary responsibility for health care. I have been a Commissioner for the Health Policy Commission in Massachusetts since 2012. As part of its responsibilities, the Commission has extensively studied the impact of opioid use on the health of citizens and the cost of medical care in Massachusetts and has sponsored programs to reduce the impact of opioids.

5. I have written extensively on issues related to population health. In a number of research papers I have sought to understand how and why population health changes over time. This includes measures of fatal and non-fatal health and behavioral and economic contributors to these trends. Included in this writing are several papers on addictive goods, including analyses of smoking, obesity, and other addictive behaviors.² My current research includes analysis of the role of supply and demand factors on opioid use.

¹ Wagstaff, Adam and Anthony J. Culyer. “Four decades of health economics through a bibliometric lens.” *Journal of Health Economics* 31 (2012): 406-439, Table 5.

² Cutler, David M. and Susan T. Stewart. “The Contribution of Behavior Change and Public Health to Improved US Population Health.” Review of Behavioral and Social Sciences Research Opportunities: Innovations in Population Health Metrics. AHRQ Publication. 2015. 15(002); Cutler, David, Angus Deaton, and Adriana Lleras-Muney. “The Determinants of Mortality.” *The Journal of Economic Perspectives* 20 (2006): 97-120.; Cutler, David M., Edward L. Glaeser, and Jesse M. Shapiro. “Why Have Americans Become More Obese?” *The Journal of Economic Perspectives* 17 (2003): 93-118.; Cutler, David M., Amber I. Jessup, Donald S. Kenkel, and Martha A. Starr. “Economic Approaches to Estimating Benefits of Regulations Affecting Addictive Goods.” *American Journal of Preventative Medicine* 50 (2016): S20-S26.

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6. I submitted an expert report on behalf of plaintiff jurisdictions in the CT1 phase of this litigation in March 2019 and was deposed in April 2019. My testimony in that case evaluated, among other things, (i) the share of harms, such as crime, mental health services and child welfare services attributable to opioids; and (ii) the impact of shipments of prescription opioids on mortality from licit and illicit opioids. In January 2021, I submitted an expert report on related topics on behalf of plaintiff Washington State in its case against distributors.

7. My curriculum vitae, which provides additional detail about my career and publications, is attached as Appendix 1. My billing rate in this matter is \$900 per hour. My compensation is not dependent on the outcome of this proceeding. My analysis is ongoing, and I reserve the right to supplement or modify it based on new materials or testimony that may become available to me, including, but not limited to, other expert witness reports that have not been produced prior to the completion of my assignment, or additional discovery produced by the parties in this litigation. A list of the materials I have relied upon in formulating my opinions is attached as Appendix 2.

8. I have been asked by counsel in the MDL litigation to evaluate the following questions from an economic perspective:

- What has been the impact of the opioid crisis on the health and well-being of citizens in the U.S.?
- What is the relationship between the supply of prescription opioids and the growth of opioid-related mortality and other opioid-related harms?
- What is the relationship between the supply of prescription opioids and the growth in harms from illicit opioids – such as heroin and fentanyl – since 2010?

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- To what extent are the harms from opioids attributable to factors such as depression, despair, and social isolation?
- Do economic and demographic factors explain the wide variation in per capita dispensing and shipments across states and counties?
- From an economic perspective, can multiple parties (e.g., manufacturers, distributors, and dispensers) all be responsible for the same harms?
- How much of the harms from opioids can be attributed to various entities in the opioid supply chain, including manufacturers, distributors, and dispensers of prescription opioids?
- To what extent has defendants' misconduct caused harms in Lake and Trumbull counties?

9. Much of my analysis focuses on mortality due to opioid overdoses, the costliest social harm resulting from the opioid crisis. Specifically, I analyze statistically how shipments of prescription opioids contributed to the growth of opioid-related mortality in the United States. I also evaluate the relationship between shipments of prescription opioids and a variety of other opioid-related harms including opioid use disorder, heroin use disorder, neonatal abstinence syndrome, foster care placements, and opioid-related inpatient hospitalizations and emergency department visits.

10. My major conclusions regarding the national opioid crisis are as follows:

- Opioid use is a national public health crisis that has resulted in increased mortality, opioid use disorder (OUD), heroin use disorder (HUD), neonatal abstinence

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syndrome (NAS), foster care placements, and opioid-related inpatient hospital admissions and emergency department visits.

- Shipments of prescription opioids increased dramatically between 1997 and 2010, with wide variation in per capita shipments across states and counties over this period. Little of this variation is explained by economic or demographic factors, indicating that many shipments are unrelated to medical need.
- There is a causal relationship between the growth of prescription opioid shipments and mortality from prescription opioids. States and counties that received more shipments per capita experienced significantly greater growth in prescription opioid mortality through 2010 (prior to the growth of illicit opioid mortality). To the extent that firms in the supply chain failed to meet their obligations to accurately represent the risks associated with the products and/or failed to maintain effective controls against diversion, their misconduct had a causal relationship to mortality from prescription opioids.
- The transition from prescription to illicit opioids as the largest contributor to opioid-related harms is a direct result of the surge in prescription opioid shipments in the 2000s, combined with efforts later put in place to restrict their use. Thus, there is a causal relationship between shipments of prescription opioids and the growth in illicit opioid mortality after 2010, including in Lake and Trumbull Counties. To the extent that manufacturers, distributors, and dispensers failed to meet their obligations to accurately represent the risks associated with the products and/or failed to maintain effective controls against diversion, their

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misconduct had a causal relationship to the growth in mortality from illicit opioids after 2010, including in Lake and Trumbull Counties.

- There is a causal relationship between shipments of prescription opioids and other social harms, including OUD, HUD, NAS, foster care placements, and opioid-related inpatient hospital admissions and emergency department visits.
- “Demand side” factors such as physical pain, depression, despair, and social isolation explain only a modest portion of the increases in opioid-related mortality. Misconduct on the part of various parties in the production, distribution, and dispensing of opioids matter far more for opioid harms.
- From an economic perspective, multiple parties – including dispensers, distributors, and manufacturers of prescription opioids – can contribute to opioid-related harms by failing to identify suspicious prescriptions or shipments.

11. Chapter 1 of this report, which includes Sections II-VI, addresses the origins of the opioid crisis and the impact of opioids on mortality and other social harms from a national perspective:³

- Section II provides background on the opioid epidemic and outlines an economic framework for evaluating the effect of shipments of prescription opioids on social harms.

³ The analysis presented in this report relies largely on state-level data. Whenever possible, I have also undertaken the same analysis using data for 405 large counties for which shipment and mortality are available. Results based on county-level data are included in Appendices 5, 7, and 9.

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- Section III describes the three phases of the opioid crisis and discusses the key national trends in shipments of prescription opioids, opioid-related mortality, and other opioid-related social harms over these periods.
- Section IV establishes that shipments of prescription opioids caused both the growth in prescription opioid mortality prior to 2010 and the growth in illicit opioid mortality after 2010.
- Section V establishes that the other opioid-related harms described in Section III, including OUD, HUD, NAS, opioid-related emergency room visits and inpatient stays, and foster care placements, were caused by shipments of prescription opioids.
- Section VI establishes that the supply of prescription opioids, not demand side factors, is the principal driver of increases in opioid mortality and other opioid-related harms.

12. Chapter 2, which includes Sections VII-X, evaluates the evolution of the opioid crisis in Lake and Trumbull Counties in Ohio as well as the impact of defendants' misconduct on mortality in these counties. I understand defendants in CT3 are pharmacies that both dispensed and distributed prescription opioids.

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Chapter 1: The Opioid Crisis in the U.S. - Causes and Impact

II. Background and Economic Framework for Evaluating Causes of the Opioid Epidemic

A. Overview of Economic Harms Due to the Opioid Crisis

13. The scope and duration of opioid abuse has few precedents as a public health crisis in the U.S. More than 590,000 Americans died from opioids between 2000 and 2019, including more than 400,000 since 2010 alone. In 2019, roughly 53,100 Americans died from opioid-related overdoses⁴, which reflects 19.8 of every 100,000 adults. Opioid-related deaths in 2019 exceeded the number that died in automobile accidents or by firearms, and exceeded the number who died due to HIV at the peak of that epidemic in the U.S.⁵ The escalating opioid crisis has contributed to declines in life expectancy in the U.S. for the first time since World War II.⁶

14. The size of other drug crises in U.S. history pale in scope compared to the current opioid crisis. In contrast to the 53,100 opioid-related deaths in 2019, fewer than 3,000 individuals annually died of crack cocaine overdoses at the height of that epidemic in the late 1980s.⁷ There were 7,525 deaths involving methamphetamines (and not opioids) in 2019, just

⁴ While complete mortality data are not yet available, preliminary estimates indicate that annual opioid mortality has increased further in 2020. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

⁵ The National Highway Traffic Safety Administration reported 36,096 deaths in motor vehicle accidents in 2019. <https://www.nhtsa.gov/press-releases/roadway-fatalities-2019-fars>. NCHS mortality data accessed on CDC Wonder identify approximately 40,000 deaths were due to firearms in 2019. H.I.V. related deaths peaked in 1995 at approximately 43,000 and gun deaths in 2017 – the peak year to date – were approximately 40,000.

⁶ NCHS Data Brief No. 38, “Mortality in the United States, 2017,” November 2018, available at <https://www.cdc.gov/nchs/data/databriefs/db328-h.pdf>; Katz, Josh and Margot Sanger-Katz, “‘The Numbers Are So Staggering.’ Overdose Deaths Set a Record Last Year,” *The New York Times*, November 29, 2018, available at, <https://www.nytimes.com/interactive/2018/11/29/upshot/fentanyl-drug-overdose-deaths.html?smtyp=cur&smid=tw-nytimes>.

⁷ NCHS mortality data accessed on CDC Wonder; U.S. General Accounting Office, “The Crack Cocaine Epidemic: Health Consequences and Treatment,” January 1991, p. 14, available at <https://www.gao.gov/assets/90/89031.pdf>.

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15 percent of the opioid-related total.⁸ Similarly, there were 3,886 deaths involving cocaine (and not opioids) in 2019, just 8 percent of the opioid-related total.⁹

15. Overdose deaths are the most socially costly and dramatic manifestation of the opioid crisis. A 2017 study by the President's Council of Economic Advisors (CEA) estimates that the economic cost of fatalities from opioid overdoses in the United States in 2015 alone was over \$430 billion, based on standard estimates of the value of a statistical life used by the government in policy analysis.¹⁰ However, the economic consequences of the opioid crisis extend beyond mortality-related costs. For example:

- The CEA estimates that opioid misuse resulted in additional nationwide costs of \$72.3 billion in healthcare costs, criminal justice costs, and lost productivity annually.¹¹
- In a 2019 report, the Society of Actuaries estimated the total economic burden of opioids in the U.S. was at least \$631 billion between 2015 and 2018, including excess health care spending of \$205 billion, mortality costs of \$253 billion, criminal justice costs of \$39 billion, child and family assistance costs of \$39 billion, and lost productivity costs of \$96 billion.¹²

⁸ NCHS mortality data accessed on CDC Wonder. Data exclude methamphetamine deaths that also involved opioids. Another 8,642 overdose deaths in 2019 involved both methamphetamines and opioids.

⁹ NCHS mortality data accessed on CDC wonder. Data excluded cocaine deaths that also involved opioids. Another 11,997 overdose deaths in 2019 involved both cocaine and opioids.

¹⁰ The Council of Economic Advisors. "The Underestimated Cost of the Opioid Crisis." (2017) ("CEA (2017)"), p. 6.

¹¹ CEA (2017), Table 2.

¹² Society of Actuaries, "Economic Impact of Non-Medical Opioid Use in the United States," October 2019, p. 4.

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- Florence, et al. (2016) estimate increased nationwide health care costs from opioid abuse of \$28.9 billion, increased criminal justice costs of \$7.6 billion, and lost productivity from OUD of \$20.4 billion for 2013 alone.¹³
- Winkelman, et al. (2018) estimate that excess Medicaid costs due to NAS were \$462 million in 2014, and more than \$2 billion over a ten-year period of 2004-2014.¹⁴

16. It is difficult to estimate with precision the full social costs caused by the opioid crisis, including, for example, harms to children placed in foster care due to a parent's opioid addiction, harms to children born with NAS, and costs associated with addiction that goes untreated. Nonetheless, my analysis and related economic literature confirm that opioid-related harms other than mortality are substantial and resulted from shipments of prescription opioids.

B. Overview of Phases of the Opioid Epidemic

17. The nature and scope of the opioid crisis changed dramatically over time and my analysis identifies three distinct phases of the crisis. The precise timing of these phases can vary by state or region, depending on when the market reforms and related events that occurred during "Phase 2" were enacted.¹⁵

¹³ Florence, Curtis S., Chao Zhou, Feijun Luo, and Likang Xu. "The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013." *Medical Care* 54 (2016): 901-906 ("Florence, et al (2016)"); Table 3.

¹⁴ Winkelman, Tyler N.A., Nicole Villapiano, Katy B. Kozhimannil, Matthew M. Davis and Stephen W. Patrick. "Incidence and Costs of Neonatal Abstinence Syndrome Among Infants With Medicaid: 2004-2014." *Pediatrics* 141 (4) (April 2018). <https://doi.org/10.1542/peds.2017-3520>. ("Winkelman, et al. (2018)")

¹⁵ These three phases are also described in Maclean et al. (2020): Maclean, Johanna, Justine Mallatt, Christopher J. Ruhm, and Kosali Simon, "Review of Economic Studies on the Opioid Crisis," *NBER Working Paper* 28067, November 2020. The CDC similarly describes "three waves of opioid overdose deaths": CDC, "Understanding the Epidemic", <https://www.cdc.gov/drugoverdose/epidemic/index.html>.

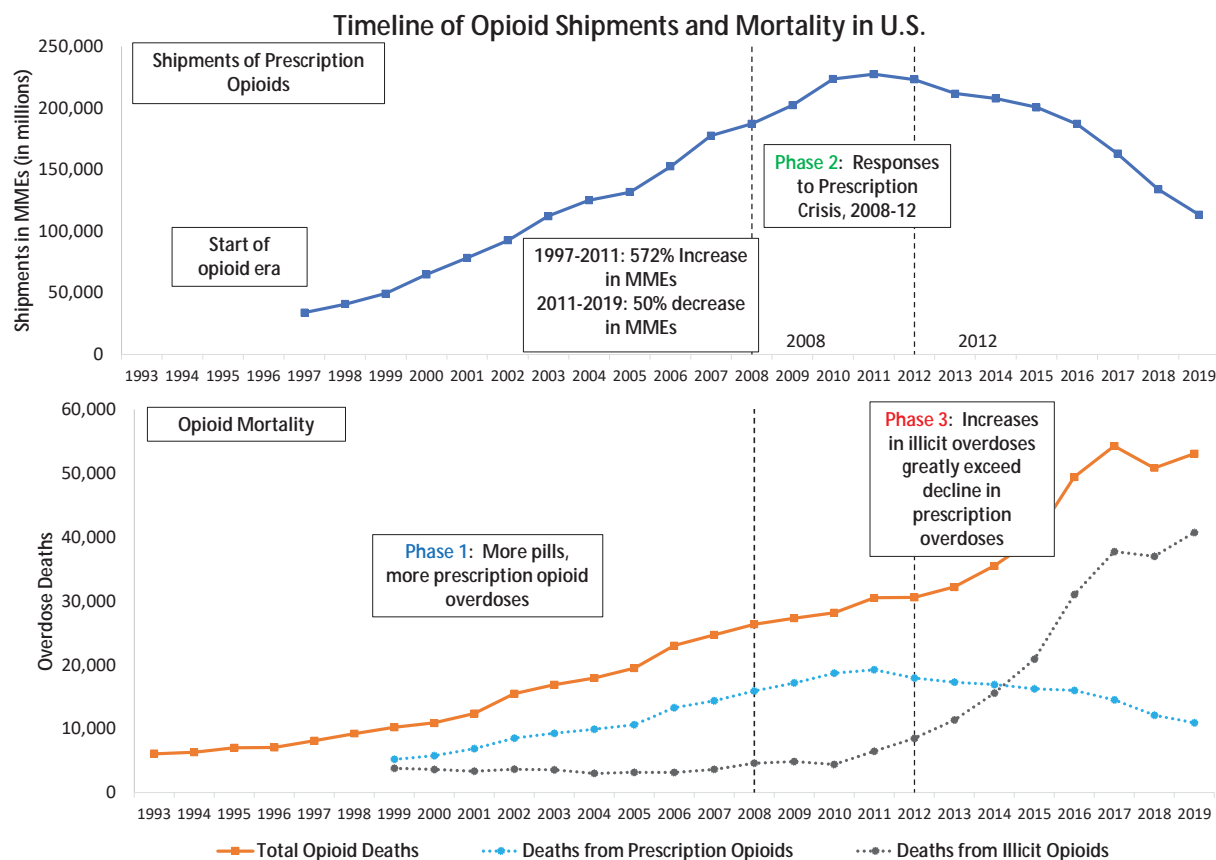
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- Phase 1 started in the mid-1990s and extended (approximately) through 2010-11. This phase was characterized by rapid increases in shipments of prescription opioids and subsequent increases in mortality and morbidity associated with prescription opioids.
- Phase 2 roughly covers the period when recognition of the opioid crisis led to policy responses, which in turn led to increased restrictions and regulatory oversight of prescription opioids and the introduction of an abuse-deterrent reformulation of OxyContin. The timing of these reforms varied across states but Phase 2 (approximately) covers 2008-12 and thus overlaps Phases 1 and 3 as I define them here.
- Phase 3 started in (approximately) 2010-11 and continues today. It is characterized by declining shipments of prescription opioids and declines in prescription opioid mortality but explosive growth in mortality due to illicit opioids including heroin and later illicit fentanyl.

18. Exhibit 1 below summarizes these phases of the crisis. The top panel of Exhibit 1 reports aggregate shipments of opioids in the U.S. between 1997 and 2019. Shipments are shown as morphine milligram equivalents (MMEs), a metric that expresses the strength of different opioid drugs in standardized units of opioid content. As the figure indicates, shipments increased by 572 percent between 1997 and 2011, the peak year for shipments nationwide. Shipments then began to decline, falling 50 percent between 2011 and 2019. The exhibit also identifies key events affecting aggregate opioid shipments over this period.

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Exhibit 1



19. The bottom panel of Exhibit 1 summarizes opioid-related mortality for 1993 through 2019.¹⁶ While mortality is not the only measure of opioid-related harms, the CEA's 2017 analysis identifies it as the primary source of economic harms due to opioids. Indeed, mortality is one of the most important and socially costly effects of the opioid epidemic and thus it is a particular focus of attention in this report. The exhibit reports three measures of opioid-related mortality – one for deaths involving prescription opioids; another for deaths involving illicit opioids (heroin and fentanyl); and another for total opioid mortality, which reflects the sum of the other two measures.¹⁷

¹⁶ The type of opioid involved in opioid-related deaths is only available in data beginning 1999.

¹⁷ Deaths involving both prescription and illicit opioids are classified as illicit. Fentanyl is available as a prescription drug but, as discussed further in Section III.C. below, the dramatic rise in fentanyl-related mortality is widely attributed to illicit fentanyl that is not distributed as prescription medication. There are few deaths involving fentanyl prior to 2012 and these deaths are classified as prescription-related; most deaths involving fentanyl in

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20. As the exhibit shows, prescription opioid mortality in the U.S. rose 218 percent from 1999 through 2010 while mortality related to illicit opioids (primarily heroin) remained relatively stable.¹⁸ After 2010, and roughly coincident with the decline in shipments of prescription opioids, mortality associated with prescription opioids started to fall; however, mortality associated with illicit opioids increased substantially from 2010 through 2017 before declining modestly in 2018 and subsequently ticking back up again in 2019. While comprehensive national data are not yet available post-2019, preliminary data indicate that opioid-related mortality in the U.S. has increased again in 2020.¹⁹

21. As demonstrated in Section IV, the rapid growth in prescription opioid mortality between 1999 and 2010, as well as the growth in illicit opioid mortality after 2010, are both causally related to shipments of prescription opioids prior to 2010 and the decline in such shipments after 2010.

22. Opioid use and opioid-related mortality in the U.S. is, according to Ho (2019), “unprecedented... compared to the experiences of other high-income countries.”²⁰ She shows that, due in large part to opioid overdoses, drug overdose rates in the U.S. far exceed those in other developed countries:

While the US is not alone in experiencing increases in drug overdose mortality, the magnitude of the differences in levels of drug overdose mortality is staggering.

2012 and later years are classified as illicit. The methods used to identify opioid-related mortality and to account for deaths with unclassified drugs are described in Appendix 3.

¹⁸ It is not possible to distinguish opioid-related mortality by type prior to 1999 due to changes in the classification of death used by the NCHS.

¹⁹ The CDC Provisional Drug Overdose Death Counts for the 12-month period ending in May 2020 were the highest on record with 79,251 total overdose deaths. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. Friedman et al. (2020) find that overdose-related cardiac arrest incidents were up as much as 125 percent in the summer of 2020 relative to 2018-2019 levels. Friedman, Joseph, Leo Beletsky, and David L. Schriger, “Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic,” *JAMA Psychiatry*, Published Online, December 3, 2020.

²⁰ Ho, Jessica Y. “The Contemporary American Drug Overdose Epidemic in International Perspective,” *Population and Development Review*, vol. 45, no. 1 (March 2019): 7-40 (“Ho (2019)”), at p. 23.

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Drug overdose mortality is now 3.5 times higher on average in the US than other high-income countries. It is over 27 times higher than in Italy and Japan, which have the lowest drug overdose death rates, and 60 percent higher than in Finland and Sweden, the comparator countries with the next highest death rates.²¹

23. Using data from the United Nations International Narcotics Control Board, Keith Humphreys of Stanford University finds that prescription opioid consumption per capita in the U.S. is the largest among world nations. He notes that “Americans are prescribed about six times as many opioids per capita as are citizens of Portugal and France, even though those countries offer far easier access to health care.”²²

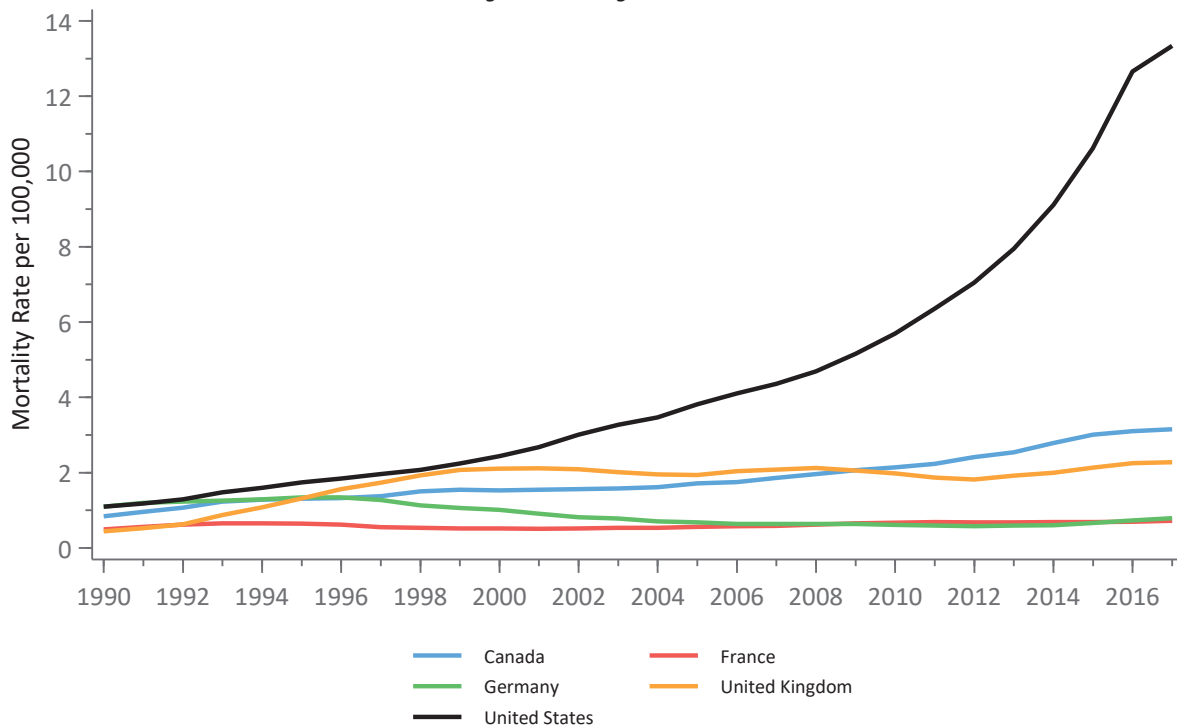
24. Data on opioid overdose mortality rates in major western countries from the Institute for Health Metrics and Evaluation at the University of Washington are reported in Exhibit 2. As the figure indicates, the opioid mortality rate (per 100,000) has grown much more rapidly in the U.S. than in Canada, the United Kingdom, France, and Germany since 1990. To cite one example, in 1999, the opioid mortality rate in the U.S. exceeded that in France by 1.7 per 100,000. By 2017, the U.S. rate exceeded that in France by 12.6 per 100,000.

²¹ Ho (2019), at p. 24.

²² Humphreys, Keith, Stanford University, “Americans use far more opioids than anyone in the rest of the world,” *Washington Post*, March 15, 2017, <https://www.washingtonpost.com/news/wonk/wp/2017/03/15/americans-use-far-more-opioids-than-anyone-else-in-the-world/>.

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Exhibit 2

Mortality Rate from Opioid Use Disorder
By Country, 1990-2017

Source: Institute for Health Metrics and Evaluation (IHME), Global Burden of Disease Study 2017.

C. Framework for Evaluating the Effect of Prescription Opioids on Social Harms

25. The opioid crisis has resulted in a broad range of social harms across the U.S., including, among others, addiction, mortality, morbidity, NAS, and family dissolution. An analysis of the link between opioid supply and opioid-related harms requires accounting for the unique features of the opioid marketplace. First, prescription opioids are typically classified as Schedule II controlled substances, which are drugs that have a high potential for abuse and dependence.²³ Second, prescription opioids are closely related chemically to illicit opioids

²³ U.S. Department of Justice Drug Enforcement Administration, "Drugs of Abuse 2017," available at https://www.dea.gov/sites/default/files/drug_of_abuse.pdf, p. 9. While some opioids based on hydrocodone and codeine were classified as Schedule III at various periods relevant to this analysis, these categories constitute fewer than 21 percent of MMEs shipped between 1997 and 2019.

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including heroin.²⁴ Third, some prescription opioids are distributed through illicit channels. This includes prescription opioids that are diverted from medical uses; unauthorized importation of medications such as fentanyl, which is also available on a prescription basis; and the manufacture and distribution of counterfeit medications. Moreover, and as discussed in more detail in Section III.C. below, prescription opioids often have been a “gateway” for illicit opioid use. A central feature of my analysis establishes the causal link between (i) the emergence of the illicit opioid crisis after 2010 and (ii) shipments of prescription opioids in years prior to 2010. My analysis explicitly considers how manufacturers’, distributors’, and dispensers’ failures to prevent diversion contributed to harms due to both licit and illicit opioids.

26. My framework for evaluating opioid-related harms is summarized in Exhibit 3 below, which demonstrates how, as an economic matter, multiple factors can contribute to a single result, in this case an opioid epidemic. The potential sources of misconduct are shown in the blue boxes in the upper part of the figure. I understand that manufacturers, distributors, and dispensers each have legal obligations, including those under the federal Controlled Substances Act (“CSA”), to maintain effective controls against diversion of prescription opioids, and to report suspicious prescriptions and shipments to the appropriate regulatory authorities. The actions or inactions of manufacturers, distributors, and dispensers led to dispensing and shipments of opioids, some of which were ultimately diverted to non-medical uses. As discussed in Section III.A below, there is substantial evidence that a significant share of the increases in shipments between the mid-1990s and 2010 was unrelated to medical need.

²⁴ See, for example, Kosten, Thomas R., and Tony P. George. “The neurobiology of opioid dependence: implications for treatment.” *Science & Practice Perspectives* 13 (2002): 13-20.

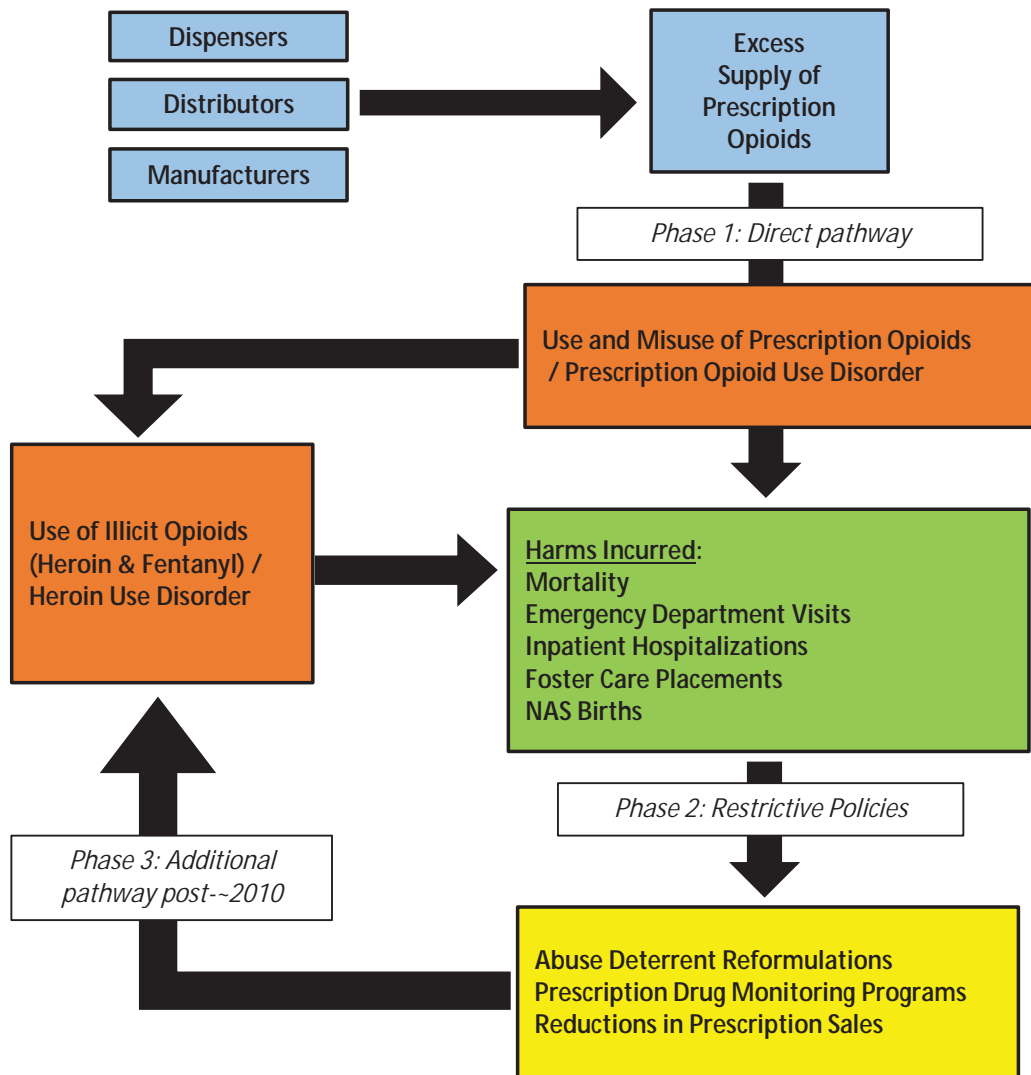
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27. While proper actions by dispensers would have reduced opioid-related harms, so too would have actions by distributors to identify and prevent suspicious shipments or actions by manufacturers to identify and disclose addiction risks associated with prescription opioid use. The blue boxes in Exhibit 3 represent how failure to maintain effective controls against diversion contributed to an excess supply of prescription opioids. The top orange box identifies how excess dispensing and shipments can lead to opioid use, misuse, and dependence. The green box identifies some additional harms resulting from dispensing and shipments of prescription opioids beyond use, misuse, and dependence. Dependence on prescription opioids in turn can translate to increased use of illicit opioids including heroin and fentanyl for individuals that lose access to prescription medications and/or users that can access illicit opioids at a lower cost than prescription opioids. This in turn creates increases in opioid-related harms. This pathway is identified in the orange box on the left side of the diagram. In addition, I understand from counsel that Plaintiffs have evidence, and intend to prove at trial, that defendants failed to identify and prevent suspicious shipments and dispensing of prescription opioids. This evidence supports the causal pathway shown in Exhibit 3.

28. In Phase 2 of the crisis, which roughly covers 2008-12, harms from prescription opioids came to be more widely recognized, leading to a variety of policy responses that restricted their availability. These restrictions then led to increased use of illicit opioids. This pathway is summarized in the yellow box at the bottom of Exhibit 3.

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Exhibit 3
Relationship Between Opioid Shipments and Harms



29. My analysis establishes that there is a causal relationship between shipments of prescription opioids and a variety of economic harms along the “direct pathway” shown in Exhibit 3. My analysis also establishes a causal relationship between the policy responses to the harms caused by excess supply of prescription opioids that started in the 2008-12 period and the increases in mortality and other harms from illicit opioids after 2010, along the “additional pathway” to harms shown in Exhibit 3. As discussed further below, this general

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framework does not imply that the opioid crisis proceeded in the same way or at the same time in every area. While local conditions can have important effects, the general framework describes general patterns in the evolution of the crisis observed both nationally and in many geographic areas.

30. My analysis, and that of others that evaluate the extent to which manufacturers, distributors, and dispensers failed to meet their legal requirements under the CSA, together can be used to approximate the extent to which harms from prescription opioids can be attributed to defendants. This general framework can be used to evaluate harms resulting from misconduct by manufacturers, distributors, and dispensers. As an economic matter, actions by firms in the supply chain could have reduced opioid-related harms and thus each group is appropriately considered to have contributed to these harms. To take an extreme example, assume that prescription opioid sales would not have increased in the absence of misconduct by manufacturers. Also assume that if dispensers had met their legal obligations, 70 percent of actual prescriptions would have been identified as suspicious and would have been stopped. In this hypothetical, 100 percent of the harms related to prescription opioids could have been avoided in the absence of misconduct by manufacturers. At the same time, 70 percent of the harms related prescription opioids could have been avoided in the absence of misconduct by dispensers. While taken together, this adds to more than 100 percent, this is an economically appropriate outcome because harms would have been reduced if any of these parties had met their legal obligations.

31. From an economic perspective, the actions of manufacturers, distributors, and dispensers each can be said to have caused opioid-related harms to the extent that they failed to meet their legal obligations, including under the CSA and other relevant laws. The law and

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economics literature recognizes that when multiple parties contribute to the same indivisible harms, legal rules that potentially make each party responsible for all harms can induce firms to take economically efficient efforts to avoid them.²⁵ This in turn implies that harms need not be uniquely associated with each responsible party in order to evaluate the impact of misconduct.

III. Phases of the Opioid Crisis

A. Phase 1: The Emergence of the Prescription Opioid Epidemic – 1995-2010

1. Shipment Trends in the U.S.²⁶

32. Opium has been used to stimulate pleasure and relieve pain for thousands of years. As early as 3400 BCE, the Sumerians referred to opium poppy at the “joy plant” and opium was well known to the ancient Greeks, Egyptians, and Persians.²⁷ Morphine became a widely used pain treatment during the 19th century, but its harmful aspects were recognized and led to the search for an ostensibly non-addictive form.²⁸ Heroin was initially introduced in the late 19th century as a non-addictive alternative to morphine, but it soon became clear that

²⁵ Landes, William M., and Richard A. Posner. “Joint and multiple tortfeasors: An economic analysis.” *The Journal of Legal Studies* 9 (1980): 517-555 explain why allowing a plaintiff to recover 100 percent of damages from a subset of contributory parties still leads to the efficient ex-ante incentives of care. Also see: Kornhauser, Lewis A., and Richard L. Revesz. “Sharing damages among multiple tortfeasors.” *The Yale Law Journal* 98.5 (1989): 831-884 (see pg. 830-31 and p. 847) and Kornhauser, Lewis., “Economic Analysis of Joint and Several Liability, *Research Handbook on the Economics of Torts* (2013), 199-233.

²⁶ My analysis uses both national data on mortality and shipments. Appendices to this report present the same analyses based on data on 405 large counties for which mortality and shipments are available between 1999 and 2019. Each of these counties have population of roughly 100,000 or more. The 405 county sample accounts for roughly 70 percent of the U.S. population and 75 percent of opioid mortality deaths as of 2018-2019.

²⁷ Trickey, Erick, “Inside the Story of America’s 19th-Century Opiate Addiction,” *Smithsonian Magazine*, January 4, 2018, available at <https://www.smithsonianmag.com/history/inside-story-americas-19th-century-opiate-addiction-180967673/>

²⁸ History.com Editors, “Heroin, Morphine and Opiates,” last updated August 21, 2018, available at <https://www.history.com/topics/crime/history-of-heroin-morphine-and-opiates>.

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heroin was addictive as well.²⁹ This resulted in early 20th century regulation in the U.S. that greatly limited the use of morphine and heroin as pain treatments.³⁰

33. The active molecule in prescription opioids has similar physiological effects to that of heroin.³¹ Throughout most of the twentieth century, physicians prescribed opioids only in limited circumstances due to addiction-related risks.³² This included palliative care and treatment of acute pain related to traumatic injuries, post-surgical care and cancer. However, in the late 1980s and early 1990s, opioids started to be prescribed more frequently for managing pain for a broader range of patients, including for treatment of chronic pain.³³ New opioids formulations were also introduced, most importantly OxyContin but others as well, and as documented by other witnesses, manufacturers and distributors encouraged the increase in opioid use. These activities resulted in a dramatic growth in the shipments of prescription opioids. Exhibit 4 shows the aggregate rise in per capita opioid shipments in the U.S. from 1997 through 2019. Data on shipments of prescription opioids from the Drug Enforcement Administration's (DEA) Automation of Reports and Consolidated Orders Systems (ARCOS) are available for 1997 and more recent years. These data indicate that shipments of prescription opioids increased by more than 500 percent between Q1 1997 and Q4 2010.³⁴ The data do not include opioids manufactured and supplied through illicit channels, including fentanyl analogs

²⁹ United Nations Office on Drugs and Crime, "History of Heroin," available at https://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1953-01-01_2_page004.html; History.com Editors, "Heroin, Morphine and Opiates," last updated August 21, 2018, available at <https://www.history.com/topics/crime/history-of-heroin-morphine-and-opiates>.

³⁰ United Nations Office on Drugs and Crime, "History of Heroin," available at https://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1953-01-01_2_page004.html.

³¹ See, for example, Kosten, Thomas R., and Tony P. George. "The neurobiology of opioid dependence: implications for treatment." *Science & Practice Perspectives* 13 (2002).

³² The history of opioid use for treatment of pain is detailed in: National Academies of Sciences, Engineering and Medicine, "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," 2017, p. 24-28.

³³ Id.

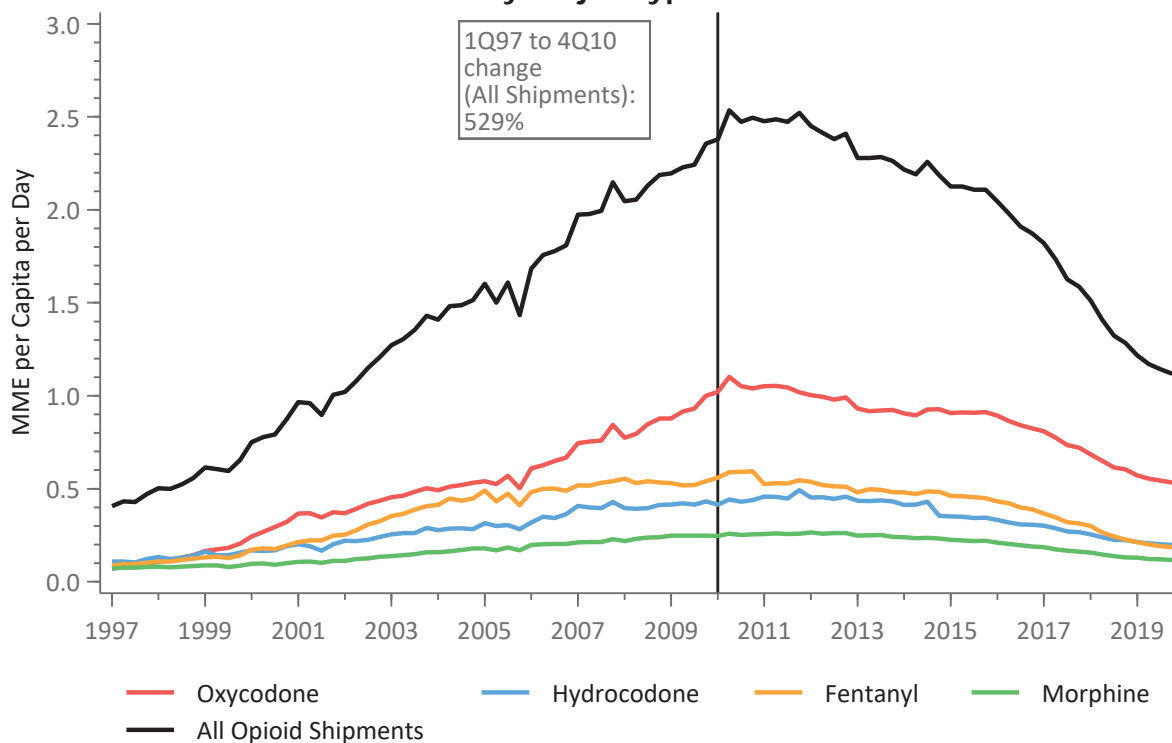
³⁴ The construction of these and other data used in this report is described in further detail in Appendix 3. Appendix 4 provides additional notes for each of the exhibits presented in this report.

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and other synthetic opioids. As discussed below, this problem has become much larger in recent years.

Exhibit 4

Shipments of Prescription Opioids in the U.S.: 1997-2019 By Major Type



Source: ARCOS.

34. As Exhibit 4 shows, the increase in shipments extended across all major classes of prescription opioids. The largest increase in shipments is for oxycodone, including Purdue Pharma's OxyContin, which increased by more than 1,400 percent between Q1 1997 and Q4 2010. Over the same period, hydrocodone shipments increased by more than 300 percent; fentanyl shipments increased by more than 600 percent; and shipments of morphine increased by 265 percent.

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2. Many Shipments of Prescription Opioids Were Unrelated to Medical Need

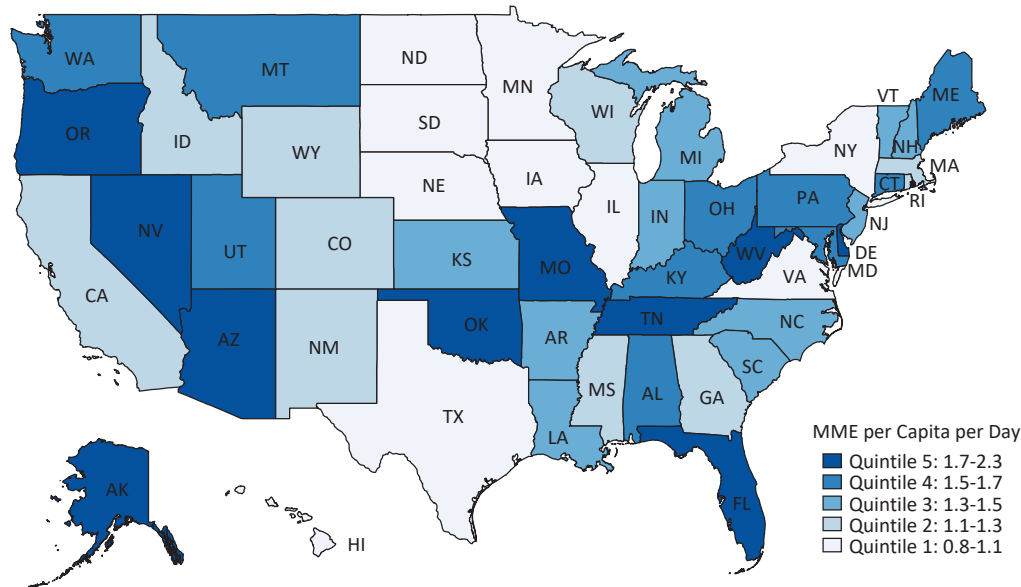
- *Wide variation across regions demonstrates that many shipments were unrelated to medical need.*

35. The dramatic growth in per capita opioid shipments between 1997 and 2010 shown in Exhibit 4 masks wide variation in per capita shipments across geographic areas. This variation is summarized in Exhibit 5 which compares average annual per capita shipments across states over the period of 1997-2010. The different colors identify the different quintiles of the distribution of per capita shipments across states, with darker colors identifying the states with higher per capita shipments. As the map indicates, the highest per capita shipments occurred in (i) the cluster of states that includes Oklahoma, Missouri, Tennessee, and West Virginia; (ii) the cluster of states that includes Oregon, Nevada, and Arizona; (iii) Florida; (iv) Delaware; and (v) Alaska. Over the 1997-2010 period, the states in the highest quintile had per capita shipments that were 94 percent larger than the average among the states in the lowest quintile. Even Exhibit 5 understates the variation in per capita shipments across geographic areas because per capita shipments also vary within states.

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Exhibit 5

Shipments of Prescription Opioids in the U.S.: 1997-2010 Average



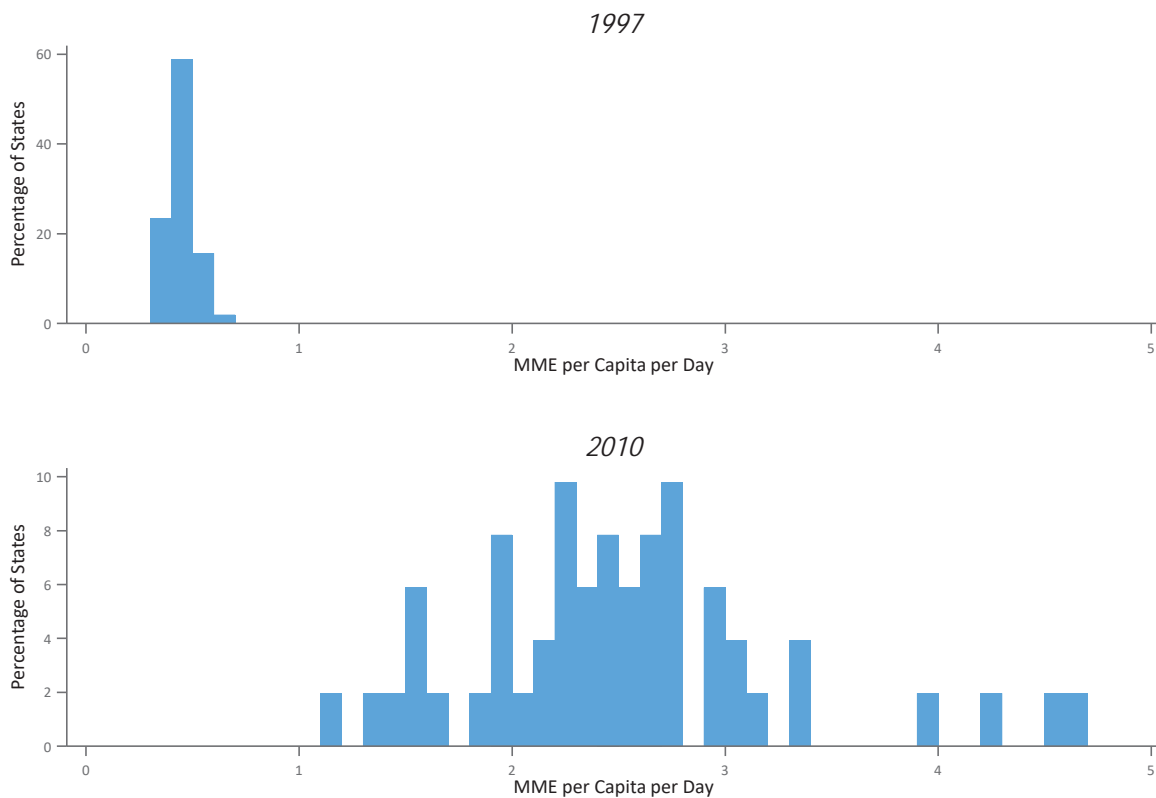
Note: Ohio ranked 15th among states for 1997-2010 shipments.
Source: ARCOS and Census Data.

36. Exhibit 6 summarizes changes in the distribution of opioid shipments across U.S. states between 1997 and 2010. As the exhibit shows, both the level of per capita shipments and the variation across states in per capita shipments increased dramatically between 1997 and 2010. In 2010, the *minimum* per capita shipments among states was more than 56 percent greater than the *maximum* state rate in 1997. The gap between the states with the highest and lowest levels of per capita shipments grew from 0.4 MMEs per person per day in 1997 to 3.5 MMEs per person per day in 2010.

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Exhibit 6

Changes in the Distribution of Per Capita Opioid Shipments Across States: 1997 and 2010



Source: ARCOS Data; U.S. Census Data.

37. Some variation in per capita shipments across states is expected due to differences in pain management needs, which are correlated with the demographic characteristics of the population. For example, a state with an older population would be expected to have greater demand for prescription opioid pain medications. However, differences in the demographic and economic characteristics of states explain little of the observed differences in per capita shipments.

38. To evaluate the extent to which variation in per capita shipments can be explained by such factors, I use regression analysis to analyze the relationship between the demographic characteristics of states and state-level shipments per capita in 2010. The

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demographic characteristics I consider are percent of state population that is male; percent white; percent under age 30; percent ages 30 to 64; the share of population with less than a high school education; prime age male employment to population ratio; and median household income. This set of factors is consistent with economic literature which has analyzed the relationship between prescription opioid supply and opioid-related mortality.³⁵ This regression is then used to construct adjusted measures of per capita shipments that control for these demographic differences and their relationship to shipments across states.³⁶

39. The analysis indicates that economic and demographic factors explain little of the variation in per capita shipments across states. The regression results are reported in Appendix 5. At the 10th and 90th percentile of the distribution, MMEs per capita per day across states were 1.65 and 3.37 respectively, a gap of 1.73 MMEs per capita per day. After accounting for the relationship between shipments and demographic characteristics, the adjusted gap between the 10th and 90th percentile is 1.55, only 10 percent smaller than the unadjusted gap. The wide variation in per capita MME across states after controlling for differences in demographic characteristics is consistent with the conclusion that many shipments were excessive and unrelated to medical need.³⁷ This analysis is consistent with the findings of the Centers for Disease Control (CDC) in Paulozzi et al. (2014), which found large

³⁵ See, for example: Ruhm, Christopher J., "Deaths of Despair or Drug Problems?" NBER Working Paper 24188, January 2018 ("Ruhm (2018)").

³⁶ Adjusted measures of per capita shipments reflect the difference between the actual level of per capita shipments and the level expected based on regression estimates of the relationship between shipments per capita in 2010 in a state and the demographic and economic characteristics of the state.

³⁷ A parallel regression analysis based on the sample of 405 large counties is summarized in Appendix 5, which yields similar results.

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variation in opioid prescribing rates across states and concluded that the “wide variations are unlikely to be attributable to underlying differences in health status of the population.”³⁸

40. In sum, the wide variation in per capita MMEs across states after controlling for differences in demographic characteristics indicates that only a small share of the variation in shipments across states is attributable to economic and demographic characteristics of the states. The fact that little of the variation in per capita shipments can be attributed to demographic and economic factors that proxy for licit prescription opioid demand provides evidence of widespread opioid shipments unrelated to medical need.

- *NSDUH survey data establish that many shipments are unrelated to medical need*

41. Dispensing of prescription opioids unrelated to medical need is also reflected in data collected through the National Survey on Drug Use and Health (NSDUH), which documents that individuals that misuse prescription painkillers typically obtain pills from sources other than physicians.³⁹ In particular, the NSDUH survey asks respondents that have misused pain relievers in the past year to identify the source for their last non-medical use. As summarized in Exhibit 7, in 2010 doctors were the source of the most recently misused pain relievers for only 19 percent of such respondents nationally. On the other hand, 70 percent reported that their most recently misused pain reliever was purchased from a friend, family member, or dealer, or was provided free by a friend or family member. These data indicate that misuse of prescription pain killers frequently occurred due to oversupply and diversion.

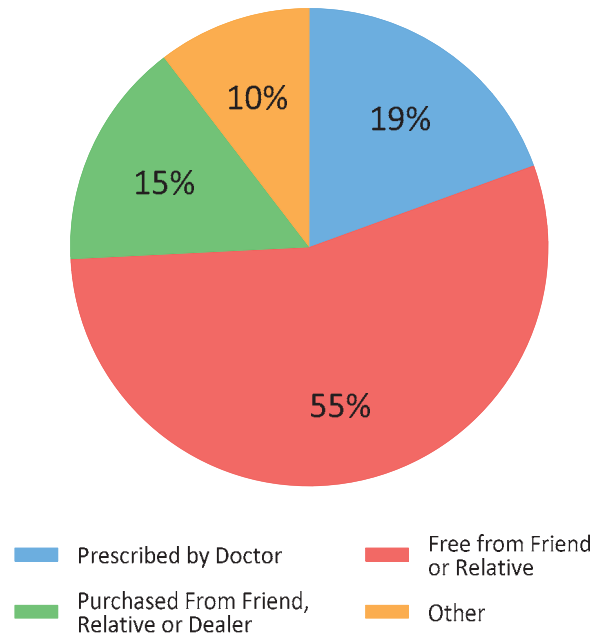
³⁸ Paulozzi, Leonard J., Karin A. Mack, and Jason M. Hockenberry, “Vital Signs: Variation Among States in Prescribing Opioid Pain Relievers and Benzodiazepines – United States, 2012,” *Morbidity and Mortality Weekly Report* vol. 63, no. 26 (July 4, 2014).

³⁹ The NSDUH Survey is undertaken by the Substance Abuse and Mental Health Services Administration (SAMHSA) of the U.S. Department of Health and Human Services. It is a nationally representative survey based on in-person interviews of roughly 70,000 households annually. https://nsduhweb.rti.org/respweb/about_nsduh.html.

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Exhibit 7

**NSDUH Survey Data Indicate that Most Recent Pain Reliever Misuse is
Diversion from Friend, Relative, or Dealer
2010**



Note: Sample includes individuals who misused prescription pain relievers within the past year.
Source: NSDUH.

3. Mortality Trends in U.S. during Phase 1

42. Opioid-related mortality is a critical measure of the harms associated with opioids. My analysis relies on Multiple Cause of Death (MCOd) data from the National Center for Health Statistics (NCHS) to evaluate trends in opioid-related mortality. These data are derived from death records issued by county officials and compiled by state officials. As explained in the Data Appendix (Appendix 3), my analysis makes adjustments for commonly recognized limitations of the MCOd data.⁴⁰ These include: (i) adjustments for changes over time in the coding of the International Classification of Diseases (ICDs); (ii) adjustments to account for overdose death records that do not specify the drug involved; and (iii) adjustments

⁴⁰ ICD codes used to classify deaths in the MCOd data were revised in 1999. In addition, MCOd data for 1998 and earlier years do not identify the type of opioid(s) that contributed to a death (e.g., prescription opioids, heroin, fentanyl, etc.). Finally, reporting practices can differ across counties and over time due to changes in drug testing procedures and other factors.

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to account for opioid-related overdoses that do not report the type of opioid involved.⁴¹ These adjustments are described in more detail in Appendix 3.

43. My analysis of post-1999 data categorizes opioid-related drug overdoses into two categories: (i) prescription opioid mortality; and (ii) illicit opioid mortality. If the MCOD data identify the presence of both prescription opioids and illicit opioids, then the death is treated as illicit. The MCOD data do not permit identification of the type(s) of opioids associated with overdose deaths prior to 1999, so only total opioid mortality is reported for 1993-1999. As discussed above, all fentanyl-related mortality is included with prescription opioids before 2013 as there is little evidence of the availability of illicit fentanyl for most of this period.⁴²

44. Some prescription opioid mortality can reflect illicit use. For example, some opioid overdoses identified as prescription-related likely result from pills obtained outside of the prescription drug distribution network (e.g., through drug dealers, family members or friends) or may be counterfeit forms of prescription medications. Moreover, some illicit opioid mortality in this period may be the consequence of dependence resulting from the prior use of prescription opioids, as discussed in more detail below.

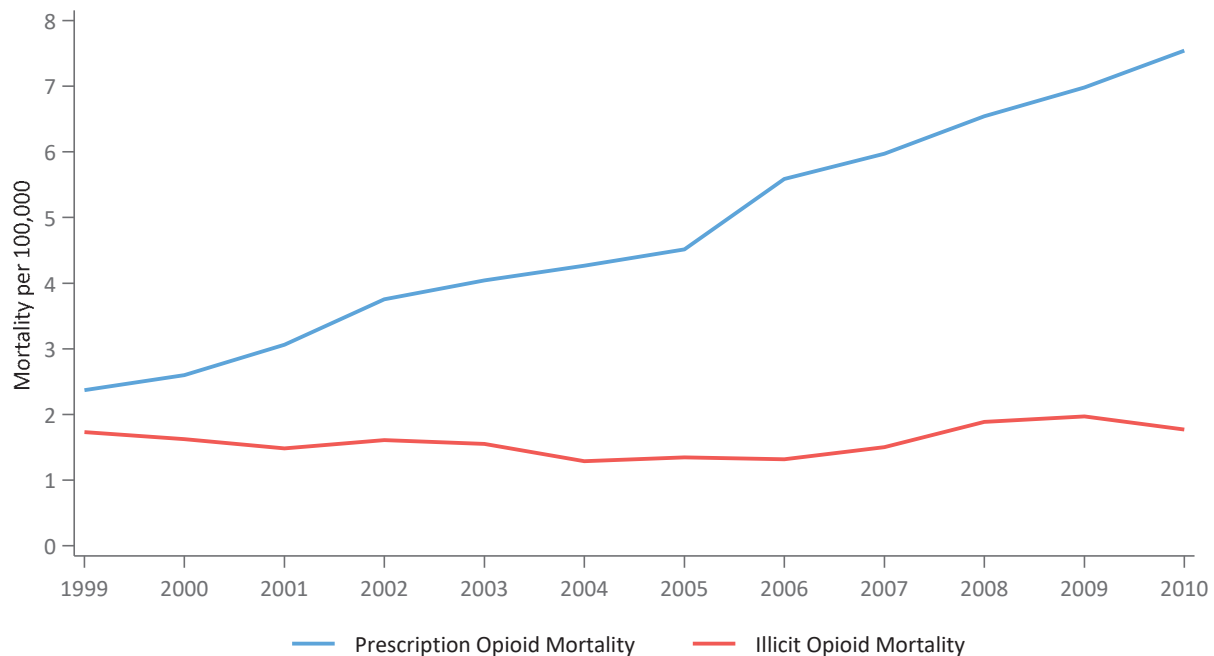
45. Exhibit 8 summarizes opioid overdose mortality rates – separately for illicit mortality and prescription mortality – for the U.S. between 1999 and 2010.

⁴¹ My analysis builds on the adjustment process developed by Christopher Ruhm. Christopher J., “Corrected US opioid-involved drug poisoning deaths and mortality rates, 1999–2015,” *Addiction* 113 (2018): 1339-1344.

⁴² Pardo et al. (2019) note that while there were a handful of earlier outbreaks of illicit fentanyl, they were “generally localized and short-lived” compared to the post-2013 period. Pardo, Bryce, Jirka Taylor, Jonathan P. Caulkins, Beau Kilmer, Peter Reuter, and Bradley D. Stein, *The Future of Fentanyl and Other Synthetic Opioids* RAND Corporation, Santa Monica, CA: 2019, at p. xvii.

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Exhibit 8

Opioid Mortality Rate by Type: 1999-2010
U.S. Total

Source: NCHS Mortality Data

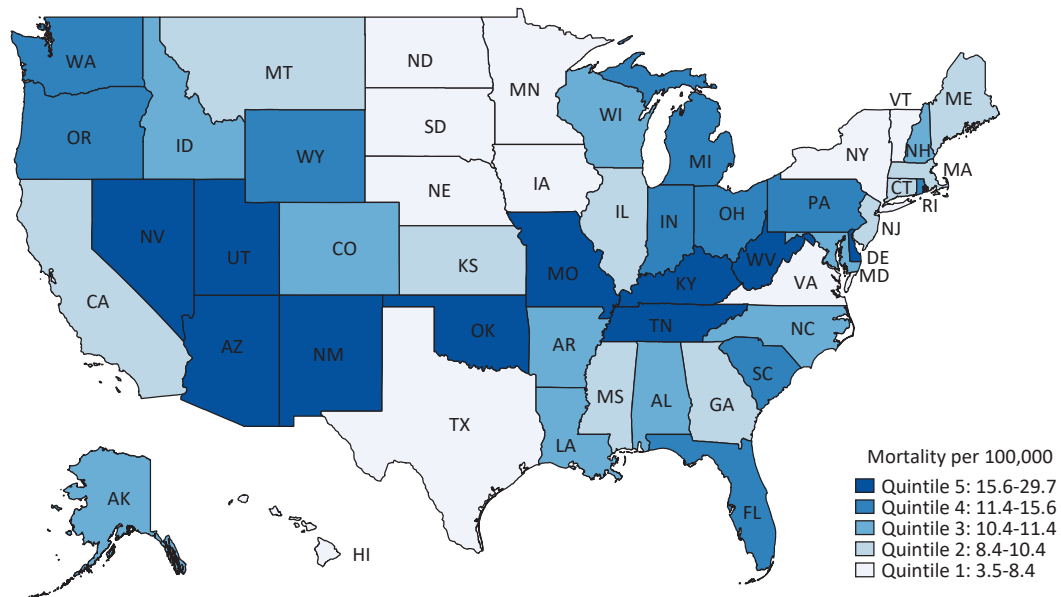
46. As Exhibit 8 indicates, nearly all of the increase in opioid mortality in the U.S. between 1999 and 2010 is attributable to the growth in prescription opioid mortality, which increased by 218 percent. Illicit opioid mortality grew only 2 percent over the period.

47. As with shipments, the national trends hide variation in mortality across different areas within the U.S. Exhibit 9 shows opioid mortality rates by state in 2010. In 2010, the states in the highest quintile had per capita mortality that was 190 percent larger than the average among the states in the lowest quintile. As the map indicates, the states with the highest per capita mortality in 2010 were (i) the cluster of states that includes Oklahoma, Missouri, Tennessee, and West Virginia; (ii) the cluster of states that includes Nevada, Arizona, Utah, and New Mexico; and (iii) Delaware. Many of these states were also the states with the highest levels of per capita shipments over the 1997-2010 period, as shown in Exhibit 5.

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Exhibit 9

Any Opioid Mortality Rates: 2010



Source: NCHS Mortality Data and Census Data.

B. Phase 2: Responses to the Prescription Opioid Epidemic – 2008-2012

48. The explosive growth in shipments of prescription opioids during the 1990s and 2000s and growing recognition of increases in opioid misuse and opioid-related mortality started to generate responses by law enforcement officials, policymakers, and industry participants. Responses included development of state Prescription Drug Monitoring Programs (PDMPs), laws regulating opioid prescription activity, and greater regulation of pain clinics.

49. State PDMP laws emerged as a response to the growth in shipments of prescription opioids and the corresponding increase in opioid-related mortality. Under PDMP laws, states collect patient-level data from prescribers and/or dispensers of prescription opioids and assemble the data into an electronic database in order to improve monitoring for, and

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prevention of, misuse.⁴³ While some states had PDMP laws predating the opioid crisis, the number of states that adopted PDMP laws grew through the 2000s, growing from 16 in 2001 to 41 in 2012.⁴⁴ At the same time, states with older PDMP laws expanded their scope.⁴⁵ Nonetheless, there are differences across states in the scope of laws. For example, physician participation in PDMPs is voluntary in some states and mandatory in others.

50. State actions extended beyond PDMP laws. Meara et al. report states added 81 new controlled substance laws between 2006 and 2012.⁴⁶ Public and private insurers also showed growing awareness of the risks of prescription opioid misuse and took steps to curtail over-prescribing and to prevent diversion.⁴⁷

51. Around the same time, legal actions started to be brought against drug distributors and manufacturers. In 2008, McKesson paid \$13 million to settle claims that it failed to report suspicious patterns of shipments as required by the DEA.⁴⁸ Also in 2008,

⁴³ Puac-Polanco, Victor, Stanford Chihuri, David S. Fink, Magdalena Cerdá, Katherine M. Keyes, and Guohua Li (“Puac-Polanco et al.”), “Prescription Drug Monitoring Programs and Prescription Opioid–Related Outcomes in the United States,” *Epidemiologic Reviews* 2020:00, pp. 1-20.

⁴⁴ Clark, Thomas, John Eadie, Peter Kreiner, and Gail Strickler (“Clark et al. 2012”), “Prescription Drug Monitoring Programs and Prescription Opioid–Related Outcomes in the United States,” Prepared for the Pew Charitable Trusts, at p. 5.

⁴⁵ Id.

⁴⁶ Meara, Ellen, Jill R. Horwitz, Wilson Powell, Lynn McClelland, Weiping Zhou, A. James O’Malley, and Nancy E. Morden (“Meara et al.”), “State Legal Restrictions and Prescription-Opioid Use among Disabled Adults,” June 2016, pp. 44-53.

⁴⁷ For example, a CDC report documents the declines in opioid prescription activity following a private insurer’s implementation of an opioid utilization policy launched in 2012. See: Centers for Disease Control and Prevention, Morbidity and Mortality “Weekly Report: Decline in Opioid Prescribing After a Private Insurer Policy Change – Massachusetts, 2011-2015 (October 21, 2016), pp. 1125-1131.

⁴⁸ DOJ Press Release, “McKesson Corporation Agrees to Pay More than \$13 Million to Settle Claims that it Failed to Report Suspicious Sales of Prescription Medications,” May 2, 2008, available at <https://www.justice.gov/archive/opa/pr/2008/May/08-opa-374.html>.

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Cardinal Health paid \$34 million to settle claims that it failed to report suspicious sales of controlled substances to the DEA.⁴⁹

52. In 2007, Purdue paid \$635 million to settle federal and civil charges for misleading claims about its addiction risks.⁵⁰ Three Purdue executives pled guilty to criminal charges related to misrepresenting the addictive risks associated with OxyContin. Also in 2007, Purdue agreed to pay \$19.5 million to 26 states and the District of Columbia to settle complaints that it encouraged physicians to overprescribe OxyContin.⁵¹

53. In response to these pressures and others, Purdue launched an abuse-deterrent formulation of OxyContin in 2010 that made it more difficult for those dependent on opioids to use it to meet their addiction-related needs. Before 2010, the time-release aspect of OxyContin could be evaded simply by crushing pills, which facilitated abuse by individuals that were dependent on opioids.⁵²

54. Dispensers also faced regulatory action due to their failures to comply with the CSA. For example, in 2009 the DEA initiated administrative proceedings for revocation or suspension of the license of a San Diego Walgreens pharmacy with allegations of failing to stop dispensing of controlled substances that were diverted. The parties entered into a Memorandum of Agreement arising from the allegations in 2011. In 2012, the DEA filed a suspension order for a Walgreen's distribution center in Jupiter, Florida and initiated

⁴⁹ U.S. States Attorney's Office Colorado, "Cardinal Health Inc., Agrees to Pay \$34 Million to Settle Claims That it Failed to Report Suspicious Sales of Widely-Abused Controlled Substances," October 2, 2008, available at https://www.justice.gov/archive/usao/co/news/2008/October08/10_2_08.html.

⁵⁰ Tesoriero, Heather Won, "OxyContin Maker Pleads Guilty --- Purdue Frederick to Pay \$634.5 Million Settlement For Hiding Addiction Risk," *The Wall Street Journal*, May 11, 2007.

⁵¹ Associated Press, "Painkiller's Maker Settles Complaint," *The New York Times*, May 9, 2007.

⁵² Goodnough, Abby and Katie Zezima, "Drug Is Harder to Abuse, but Users Persevere," *The New York Times*, June 15, 2011, available at <https://www.nytimes.com/2011/06/16/health/16oxy.html>. The abuse deterrent formulation made the drug harder to abuse as the pills turn into a gummy substance rather than powder when crushed.

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administrative proceedings for revocation or suspension of the licenses of six other Walgreens pharmacies. Walgreens subsequently paid \$80 million in a settlement with the DEA – the largest in DEA history at the time – to resolve allegations about recordkeeping and dispensing violations of the CSA.⁵³

C. Phase 3: 2010 to Present

55. The responses to the opioid crisis that occurred during Phase 2 – increased oversight of prescription activity, legal actions against manufacturers, distributors, and dispensers as well as the reformulation of Oxycontin – marked a critical turning point in the opioid epidemic. As this section demonstrates, while the responses to the crisis had the desired effect of reducing shipments of prescription opioids and prescription opioid mortality, the same events had the unintended consequence of unleashing a dramatic increase in illicit opioid use and mortality. In effect, the deck was already stacked by 2010; given the policies available, there was no way to reduce use of licit opioids without leading to a large increase in use of illicit opioids. This section describes the evolution of the opioid crisis since 2010. The causal connection between the rise of illicit opioid mortality in Phase 3 and defendants' conduct is established in Section IV below.

1. Shipments and Prescription Opioid Mortality: 2010 to Present

56. The responses to the opioid crisis had the desired effect of reducing both shipments of prescription opioids and prescription opioid mortality. As summarized in Exhibit 10:

⁵³ In RE: National Prescription Opiate Litigation, MDL No. 2804, Case No. 1:17-md-2804, Case Track Three Plaintiffs' Motion for Leave to File Amended Complaints, Exhibit B, ¶¶515-518.

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- Shipments measured in MMEs per capita in the U.S. fell 53 percent between 2010 and 2019. Nevertheless, MMEs per capita in 2019 remained 168 percent higher than in 1997, the year after OxyContin was launched.
- As discussed further below, national prescription opioid mortality fell by 46 percent between 2010 and 2019 but remained 72 percent over 1999 levels, the first year for which such data are available.

Exhibit 10
Shipments and Prescription Opioid Mortality
U.S. Total

Year	Shipments	Prescription Opioid Mortality
Rate		
1997	0.43	
1999	0.62	2.37
2010	2.47	7.54
2019	1.16	4.09
Percent Change		
1997-2010	469%	
1999-2010	300%	218%
2010-2019	-53%	-46%
1999-2019	168%	72%

Note: Shipments are measured as MME per capita per day.
Mortality is measured as opioid overdose mortality rate per 100,000 population.
Sources: NCHS Mortality Data and ARCOS.

2. Trends in Illicit Opioid Mortality in the U.S.: 2010 to Present

57. The responses to the opioid crisis – including restrictions on the availability of prescription opioids and the reformulation of OxyContin – made it more difficult for individuals dependent on opioids to meet their needs. What was not fully recognized at the time was that

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the massive increase in shipments in the 1990s and 2000s created a large population of people that had become dependent on opioids and that many such people would turn to illicit opioids – first heroin starting in 2010, and then illicit fentanyl starting in 2013.

58. Illicit opioids involve higher mortality risk than prescription opioids due in part to the fact that their MME content is non-standardized and not observed – varying across dealers and over time. Fentanyl, which is often blended with heroin, raises greater mortality risks than heroin due to its high concentration of opioids – 1 milligram of raw fentanyl is equal in potency to 100 milligrams of morphine or hydrocodone, 67 milligrams of oxycodone, or 25 milligrams of hydromorphone.⁵⁴ As a result, small variations in MME content of blends of heroin and other substances with fentanyl can significantly raise overdose risk.

59. The measurement of illicit opioid mortality is complicated by several factors. While fentanyl has long been available on a prescription basis, distribution of illicit fentanyl, much of it imported from China and Mexico, expanded rapidly after 2013. Available data, however, do not distinguish overdose deaths associated with prescription and illicit fentanyl. I treat opioid-related mortality involving fentanyl prior to 2014 as prescription-related. For 2014 and more recent years, I define “illicit opioid mortality” to include any deaths involving heroin plus deaths involving fentanyl in excess of the average rate of fentanyl deaths in 2011-13. The average of fentanyl-related deaths in 2011-13 continues to be treated as prescription-related in 2014 and later years. I also present some analyses based on heroin overdoses alone.⁵⁵

⁵⁴ Centers for Medicare and Medicaid Service, “Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors,” <https://www.cms.gov/Medicare/Prescription-Drug-coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf>, accessed June 15, 2020.

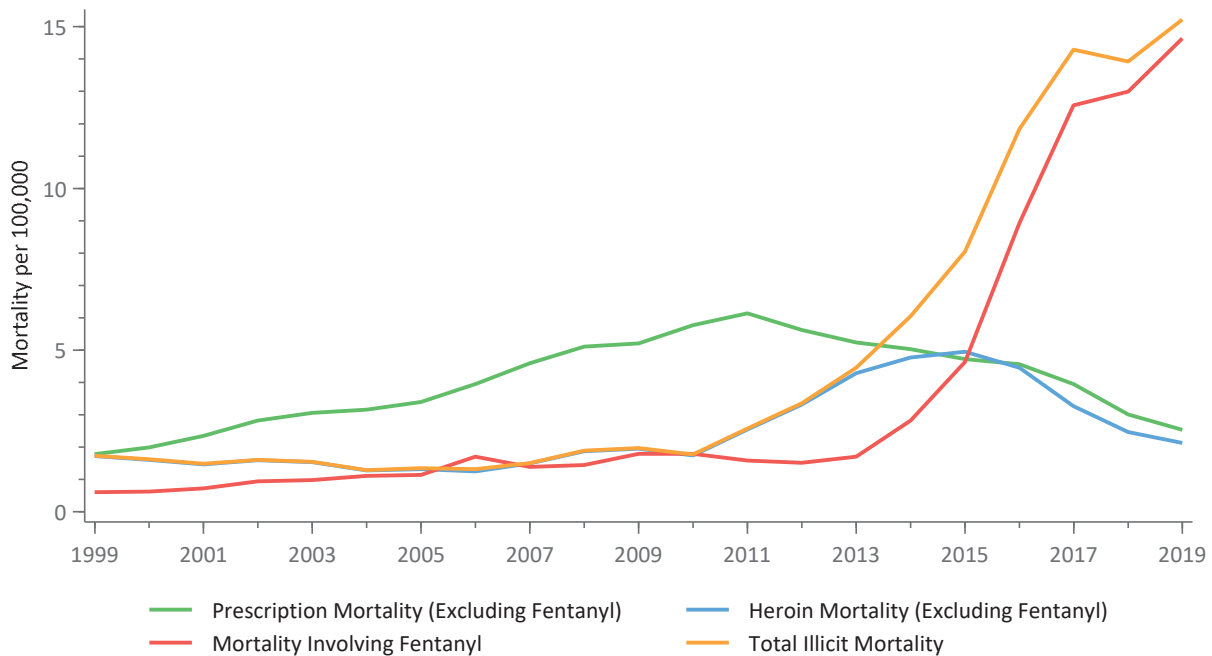
⁵⁵ As discussed in Section III.A.3 above, there is no clear distinction between prescription and illicit opioids because (i) prescription opioids can be obtained through illicit channels; (ii) substances identified as prescription drugs in

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60. Mortality rates in the U.S. from heroin and fentanyl, as well as prescription opioids, are reported in Exhibit 11, which extends the data presented in Exhibit 8 above. As the figure indicates, mortality from heroin and fentanyl has grown dramatically since 2010 while prescription opioid mortality has fallen. Heroin mortality began to accelerate in 2010 and fentanyl mortality began its dramatic increase in 2014. The decline in heroin-only mortality after 2015 reported in Exhibit 11 reflects the fact that many overdoses involve both fentanyl and heroin and these are classified as fentanyl-related. Overall, illicit opioids accounted for 16 percent of all opioid mortality in 2010; by 2019, that figure had increased to 77 percent.

Exhibit 11

Prescription and Illicit Opioid Mortality Rate: 1999-2019
U.S. Total



Source: NCHS Mortality Data and Census Data.

the MCOD data may be counterfeit; and (iii) mortality associated with illicit drugs may be the result of dependence resulting from the prior use of prescription opioids.

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61. Exhibit 12 further demonstrates the large increase in illicit mortality rates after 2010. Between 2010 to 2019 illicit opioid mortality increased by more than 750 percent while prescription opioid mortality fell by 46 percent. Over the same period, total opioid mortality – including prescription and illicit opioid mortality – increased by 75 percent.

Exhibit 12
Shipments and Opioid Mortality
U.S. Total

Year	Shipments	Mortality		
		Prescription	Illicit	Total
Rate				
1997	0.43			3.80
1999	0.62	2.37	1.73	4.67
2010	2.47	7.54	1.77	11.35
2019	1.16	4.09	15.22	19.84
Percent Change				
1997-2010	469%			199%
1999-2010	300%	218%	2%	143%
2010-2019	-53%	-46%	759%	75%
1999-2019	168%	72%	778%	325%

Note: Shipments are measured as MME per capita per day. Mortality is measured as opioid overdose mortality rate per 100,000 population.

Sources: NCHS Mortality Data and ARCOS.

62. The timing of the growth of mortality from illicit opioids and the responses to the prescription opioid crisis during Phase 2 is not a coincidence. The statistical analysis presented in Section IV below establishes the causal relationship between shipments of prescription opioids in prior periods and both prescription and illicit opioid mortality. Here, I note only that factors such as the changes in the legal and regulatory environment to reduce diversion to non-medical uses and the overall reduction in shipments and the reformulation of OxyContin resulted in prescription opioid users turning to illicit opioids to satisfy their addiction.

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63. This relationship has been identified by many others. For example, the National Academies of Science, Engineering, and Medicine noted that “[a] preponderance of evidence suggests that the major increase in prescription opioid use beginning in the late 1990s has served as a gateway to increased heroin use. [...] In addition to prescription opioids serving as a gateway to use of heroin, market forces and efforts designed to reduce harms associated with use of prescription opioid medications (e.g., ADFs) may be contributing to increased heroin use.”⁵⁶ In addition, as set forth in the expert reports of Anna Lembke and Katherine Keyes, there is a well-recognized epidemiological link between initial prescription opioid use and subsequent heroin use.

64. As discussed above, around 2014 drug traffickers started to incorporate illicit fentanyl as a lower-cost alternative to heroin.⁵⁷ Due to illicit fentanyl’s low-cost and high potency, it is often blended with heroin or otherwise sold as heroin by drug dealers. The DEA’s 2017 National Drug Threat Assessment noted that “Mexican traffickers are [...] expanding the use of highly-profitable fentanyl within white powder [heroin] markets. Because of fentanyl’s high potency, traffickers can increase their profits and heighten the potency of low-quality of heroin by mixing fentanyl with heroin.”⁵⁸ The DEA estimates that drug trafficking organizations face costs of \$5,000 - \$7,000 per kg for heroin (from Colombia) compared to fentanyl costs of

⁵⁶ National Academies of Sciences, Engineering and Medicine, “Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use,” 2017, p. 215-217.

⁵⁷ DEA Intelligence Brief, “Counterfeit Prescription Pills Containing Fentanyls: A Global Threat, DEA-DCT-DIB-021-16,” July 2016, available at https://content.govdelivery.com/attachments/USDOJDEA/2016/07/22/file_attachments/590360/fentanyl%2Bpills%2Breport.pdf, p. 2.

⁵⁸ U.S. Department of Justice Drug Enforcement Administration, “2017 National Drug Threat Assessment,” available at https://www.dea.gov/sites/default/files/2018-07/DIR-040-17_2017-NDTA.pdf, p. 54

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\$3,300 - \$5,000 per kg.⁵⁹ But one kg of fentanyl can yield 16-24 kg of final product. Thus, the price of fentanyl per use is approximately 3 percent of that for heroin.

65. When sold by drug dealers to end users, fentanyl is often mixed with heroin or sold as heroin. As the DEA notes, “[f]entanyl in these forms looks like heroin, is packaged in the same baggies or wax envelopes as heroin and displays similar stamps or brands as heroin. While many heroin users have no desire to use fentanyl, some do seek it out because of its potency.”⁶⁰ Fentanyl is also used to create counterfeit versions of prescription opioids.⁶¹ In 2015, the DEA warned of a “marked surge” in the availability of counterfeit versions of prescription opioids containing fentanyl. At that time, the DEA noted:

“[T]he shape, colorings, and markings were consistent with authentic prescription medications and the presence of fentanyl was only detected after laboratory analysis [...] The rise of fentanyl in counterfeit pill form exacerbates the fentanyl epidemic. Prescription pill abuse has fewer stigmas and can attract new, inexperienced drug users, creating more fentanyl-dependent individuals.”⁶²

66. The DEA also noted in the 2020 National Drug Threat Assessment Report that illicit opioids have spread through Western states in recent years, driven in part by the spread of “fentanyl-laced counterfeit pills,” likely due to “Mexican [traffickers] seeking to further distribute fentanyl into prescription opioid user populations.”⁶³ While earlier counterfeit pills

⁵⁹ U.S. Department of Justice Drug Enforcement Administration, “2017 National Drug Threat Assessment,” available at https://www.dea.gov/sites/default/files/2018-07/DIR-040-17_2017-NDTA.pdf, p. 62.

⁶⁰ U.S. Department of Justice Drug Enforcement Administration, “2017 National Drug Threat Assessment,” available at https://www.dea.gov/sites/default/files/2018-07/DIR-040-17_2017-NDTA.pdf, p. 59.

⁶¹ DEA Intelligence Brief, “Counterfeit Prescription Pills Containing Fentanyl: A Global Threat, DEA-DCT-DIB-021-15,” July 2016, available at https://content.govdelivery.com/attachments/USDOJDEA/2016/07/22/file_attachments/590360/fentanyl%2Bpills%2Breport.pdf, pp. 2-3.

⁶² U.S. Department of Justice / U.S. Drug Enforcement Agency, 2016 National Drug Threat Assessment Report, at p. 68.

⁶³ U.S. Department of Justice / U.S. Drug Enforcement Agency, 2020 National Drug Threat Assessment Report, at p. 12.

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containing fentanyl appeared to be pressed domestically using imported fentanyl, in 2020 the DEA noted that Mexican traffickers were pressing pills before importing them into the United States. The DEA explains that these traffickers:

“[H]ave consistently chosen to counterfeit a brand of licit 30 mg oxycodone pills that have been regularly diverted for years to the street market for opioids [...] The selection of these tablets -- blue, round, stamped with an ‘M’ on one side and ‘30’ on the other and increasingly referred to on the streets as ‘Mexican Oxy’ or ‘M30s’ – demonstrate that traffickers are taking advantage of an established market for these pills to increase the profit margins with fentanyl.”⁶⁴

67. The diminishing availability of prescription opioids after 2010 led to increases in the demand for illicit opioids, which in turn led to a corresponding increase in supply. This response resulted in further increases in opioid-related mortality and other harms, including harms to individuals that had not previously used prescription opioids. In this sense, the prescription opioid epidemic led to a “thickening” in the market for illicit drugs.⁶⁵ More specifically, increases in number of drug users reduces the costs of distributing drugs because many users expand the market by providing drugs to friends and family that might not otherwise purchase drugs from someone they don’t know. This “thickening” also results in the entry of more dealers.

⁶⁴ U.S. Department of Justice / U.S. Drug Enforcement Agency, 2020 National Drug Threat Assessment Report, at pp. 16-17.

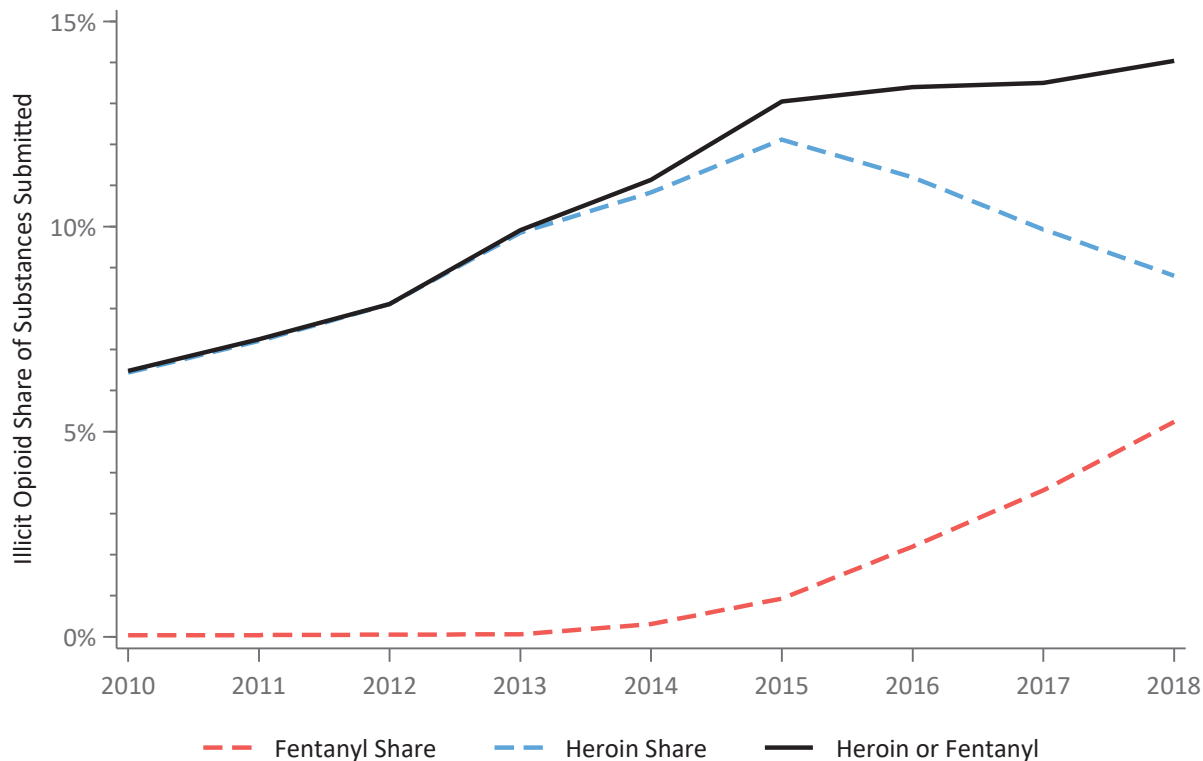
⁶⁵ National Academies of Science, Engineering, and Medicine (2021), *High and Rising Mortality Rates among Working-age Adults*. Washington, D.C.: The National Academies Press, p. 7-24. For a discussion of related concepts, see also: Chapter 2, “Markets for Drugs,” in National Research Council (2010), *Understanding the Demand for Illegal Drugs*, Washington, DC: The National Academies Press, Chapter 2 . <https://doi.org/10.17226/12976>. For further discussion of “thick” markets for illegal goods, see: Jacobson, Mireille, “Baby Booms and Drug Busts: Trends in Youth Drug Use in the United States, 1975-2000,” *The Quarterly Journal of Economics*, vol. 119 no. 4 (November 2004) pp. 1481-1512; Philip J. Cook, Jens Ludwig, Sudhir Venkatesh, and Anthony A. Breaga, “Underground Gun Markets,” *The Economic Journal*, Vol. 117 (November, 2017), pp. F558-588; Caulkins, Jonathan P. and Mark Kleinman, “Lessons to Be Drawn from U.S. Drug Control Policies,” *European Journal of Criminal Policy Resolution*, vol 24 (2018), pp. 125-144.

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68. Exhibit 13 documents one aspect of the thickening of illicit opioid markets since 2010, using data on drug confiscations by law enforcement from National Forensic Laboratory Information System (NFLIS). The share of drug confiscations involving heroin or fentanyl more than doubled (to 14 percent) between 2010 and 2018. The share of drug confiscations that involved fentanyl increased from 0.04 percent in 2010 to 5.2 percent in 2018.

Exhibit 13

**Share of U.S. Drug Confiscations Involving Illicit Opioids
2010-2018**



Source: U.S. Drug Enforcement Administration, Diversion Control Division.

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and western states dominated by black tar heroin.⁶⁷ Black tar heroin is a rock-like substance that is not easily blended with fentanyl. As a result, fentanyl is a relatively closer substitute for powder heroin than for black tar heroin. Observers attribute this to the fact that it is “fairly easy to mix white powder heroin with a powder such as fentanyl. Black tar is more distinct and harder to lace with other substances because of its stickiness and colour; mixing in white powder can put buyers off.”⁶⁸

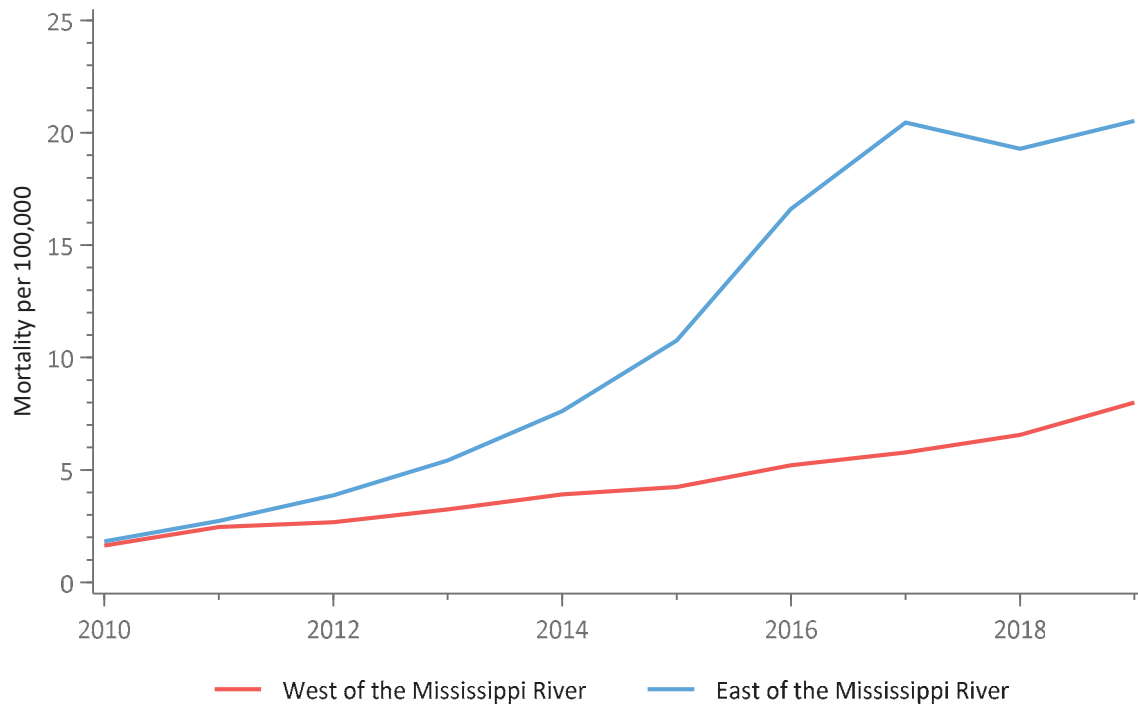
71. While the responses to the prescription opioid crisis led to greater use of illicit opioids in all regions, states east of the Mississippi River experienced larger increases than did western states. Exhibit 15 shows that illicit opioid mortality rates rose 387 percent in western states between 2010 and 2019 but grew by 1,023 percent in eastern states.

⁶⁷ U.S. Department of Justice Drug Enforcement Administration, “2017 National Drug Threat Assessment,” available at https://www.dea.gov/sites/default/files/2018-07/DIR-040-17_2017-NDTA.pdf, p. 48. Black tar heroin is a dark, rock-like form of heroin that is often produced in Mexico and sold in areas west of the Mississippi River. See <https://www.drugrehab.com/addiction/drugs/heroin/black-tar/>

⁶⁸ *The Economist*, “Inside the opioid epidemic – A selective scourge,” May 11, 2017, available at <https://www.economist.com/united-states/2017/05/11/inside-the-opioid-epidemic>.

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Exhibit 15

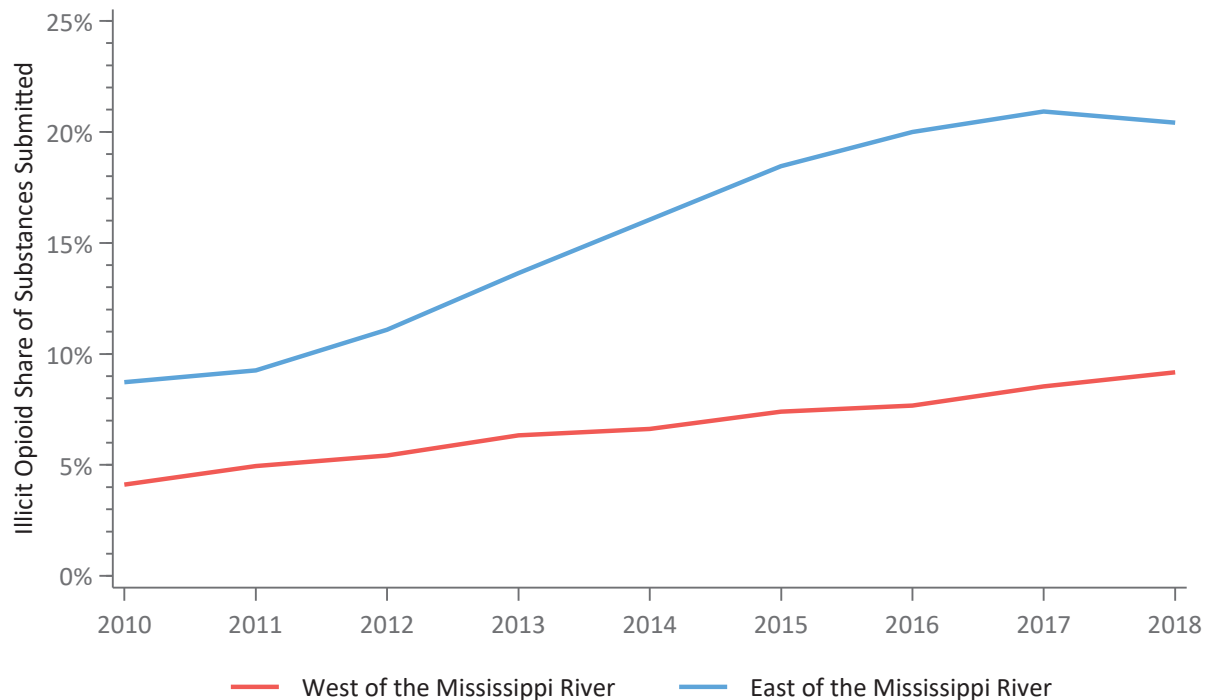
**Illicit Opioid Mortality Rate: 2010-2019
Eastern States vs. Western States**

Source: NCHS Mortality Data and Census Data.

72. A similar regional divide in the growth of the illicit opioid market is observed in drug seizure data. Exhibit 16 shows that between 2010 and 2018, the share of drug seizures accounted for by heroin and fentanyl increased by 11.7 percentage points in eastern states compared to 5.1 percentage points in western states. While region is a factor influencing the growth of illicit opioids, I establish in Section IV below that shipments of prescription opioids to an area also significantly affected the growth in illicit opioid mortality.

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Exhibit 16

Share of Drug Confiscations Identified in NFLIS Involving Illicit Opioids
Eastern States vs. Western States

Notes: Share reflects heroin and fentanyl substances included in top 60 NFLIS substances identified divided by total identified top 60 substances
 Source: U.S. Drug Enforcement Administration, Diversion Control Division.

73. As these regional differences indicate, the evolution of the opioid crisis did not proceed in the same way in all areas. While all areas experienced large increases in shipments of prescription opioids after 1995, the magnitude of those increases varied widely across areas. Further, the timing of the peak in shipments in prescription opioids was not identical in all areas: shipments peaked in 2010 in 11 states; in 2011 in 14 states; and in 2012 in 24 states. Those differences, among others, affected the demand for illicit opioids following the restrictions on prescription opioids implemented in Phase 2 of the crisis and the timing and extent of the transition to illicit opioids.

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74. Moreover, the extent of both the prescription and illicit opioid crises depend on how much diversion of prescription opioids occurred through illegal channels, which also varies across areas. For example, the diversion of prescription opioids between Florida and parts of Ohio and West Virginia via the “Oxy Express” is widely documented.⁶⁹ The extent of “arbitrage” of prescription opioids from low-price to high-price areas varied across regions and over time, depending on local supply conditions (e.g., the number of area pill mills and other factors affecting the availability of prescription opioids) and demand conditions (the number of people with opioid dependence).

75. In addition, the increased demand for illicit opioids led to a “thickening” of the market for illicit drugs that affected the abuse of non-opioid illicit drugs as well as illicit opioids. Illicit drug markets in the U.S. are served by a supply chain that includes manufacturers in the U.S., Mexico and other countries, transporters, and local distributors. Illegal drugs are often produced and distributed by “polydrug” organizations that often supply cocaine, methamphetamines, fentanyl, and marijuana in addition to heroin.⁷⁰ As noted by the DEA in 2016, “Once [heroin, methamphetamines, cocaine and fentanyl] are smuggled across the Mexican border, they are delivered to consumer markets in the United States using transportation routes and distribution cells that Mexican [traffickers] oversee both directly and indirectly. Mexican TCOs are constantly looking to expand their presence in the United States, particularly in heroin markets.”⁷¹ Thus, increases in the demand for illicit opioids created the

⁶⁹ See, for example, Quinones, Sam, *Dreamland: The True Tale of America's Opiate Epidemic* New York, NY: Bloomsbury Press, 2016, pp. 241-246.

⁷⁰ U.S. Department of Justice / U.S. Drug Enforcement Administration, 2015 National Drug Threat Assessment, p. iii.

⁷¹ U.S. Department of Justice / U.S. Drug Enforcement Administration, 2015 National Drug Threat Assessment, p. 1.

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infrastructure that contributed to increased abuse of cocaine and methamphetamines.⁷² Illicit drug traffickers also distribute fentanyl pills, which expands the use of fentanyl in markets beyond those with powdered heroin. The timing and extent of the growth in the abuse of illicit opioids and illicit drugs other than opioids varied across areas based on supply factors (including the scope of local networks for illicit drug distribution) and local demand factors.

D. Trends in Other Opioid-Related Harms

76. While mortality is a key harm for assessing the scope of the opioid crisis and the impact of defendants' misconduct, it is not the only measure of opioid-related harms. Important aspects of the opioid crisis are measured through other metrics, including OUD, HUD, NAS, opioid-related emergency department visits and opioid-related hospital inpatient admissions. Analysis of each of these metrics provides evidence of harms resulting from the opioid crisis and further establishes that areas that received more shipments realized greater harms. This section summarizes national trends in these metrics. Further analysis of these

⁷² Ellis et al. surveyed patients entering drug treatment programs in the US and concluded the "methamphetamine served as an opioid substitute, provided a synergistic high, and balanced out the effects of opioids so one could function 'normally'. Our data suggest that, at least to some extent, efforts limiting access to prescription opioids may be associated with an increase in the use of methamphetamine." (Ellis, Matthew S., Zachary A. Kasper, and Theodore J. Cicero, "Twin Epidemics: The Surging Rise of Methamphetamine Use in Chronic Opioid Users," *Drug and Alcohol Dependence* vol. 193, 2018: 14-20) The 2016 National Drug Threat Assessment of the DOJ/DEA notes: "The emergence of cocaine mixed with fentanyl in select markets is a potential trend of concern. [] Fentanyl is mixed with cocaine for the purpose of 'speedballing,' the same purpose as heroin and cocaine mixtures. The desired outcome is for the user to experience the 'high' from the cocaine with the depressant (heroin or fentanyl) helping ease the otherwise sharp comedown after the effects of the cocaine subside." (U.S. Department of Justice / U.S. Drug Enforcement Agency, 2016 National Drug Threat Assessment Report, at p. 92) The 2018 National Drug Threat Assessment of the DOJ/DEA notes: "The mixture of cocaine with fentanyl and other synthetic opioids remains a dangerous trend in an expanding number of markets. Previously, the threat was primarily concentrated in traditional cocaine markets, such as Florida, New York, Massachusetts, and Maryland; however, it has now moved beyond cocaine dominated areas into states with high opiate proliferation, such as Ohio and West Virginia. Additionally, examples of cocaine and fentanyl mixtures have been analyzed in states with neither a high synthetic opioid presence nor a high cocaine presence, such as Arkansas, Washington, and Missouri, extending the reach of both drugs outside their traditional markets." (U.S. Department of Justice / U.S. Drug Enforcement Agency, 2018 National Drug Threat Assessment Report, at p. 47)

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metrics in Section V below establishes that the underlying trends are caused by shipments of prescription opioids.

77. In addition to the harms analyzed here, economists and social scientists have also linked the opioid crisis to several additional types of harms including, crime,⁷³ child welfare outcomes (other than foster care placements),⁷⁴ labor market outcomes,⁷⁵ children and teenage suicide rates,⁷⁶ and transmission rates of hepatitis C.⁷⁷ While I do not analyze these other harms explicitly, this literature is also consistent with my conclusions that shipments and dispensing of prescription opioids (and defendants' conduct which facilitated those shipments) are causally related to the various societal harms associated with the opioid crisis.

1. Opioid Use Disorder / Heroin Use Disorder

78. The annual NSDUH survey is the basis of government estimates of opioid use disorder. The NSDUH data identify two categories of OUD – heroin use disorder (HUD) and Pain Reliever Use Disorder.⁷⁸ This evaluation is based on responses to a series of questions about

⁷³ Dave, Dhaval, Monica Deza, and Brady P. Horn (2020), "Prescription Drug Monitoring Programs, Opioid Abuse, and Crime," NBER Working Paper 24975, January 2020; Doleac, Jennifer and Anita Mukherjee (2018), "The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime," IZA Discussion Paper No. 11489, April 2018.

⁷⁴ Buckles, Kasey, William N. Evans, and Ethan M.J. Lieber (2020), "The Drug Crisis and the Living Arrangements of Children," NBER Working Paper 27633, July 2020; Evans, Mary F. Matthew C. Harris, and Lawrence M. Kessler (2020), "The Hazards of Unwinding the Prescription Opioid Epidemic: Implications for Child Abuse and Neglect," Claremont McKenna College Robert Day School of Economics and Finance Research Paper No. 3582060, April 21, 2020.

⁷⁵ Park, Sujeong and David Powell (2020), "Is the Rise in Illicit Opioids Affecting Labor Supply and Disability Claiming Rates?" NBER Working Paper No. 27804, September 2020; Krueger, Alan B. (2017), "Where Have All the Workers Gone? An Inquiry into the Decline of the U.S. Labor Force Participation Rate," Brookings Papers on Economic Activity, BEPA Conference Drafts, September 7-8, 2017; Harris, Matthew, Lawrence Kessler, Matthew Murray, and Beth Glenn (2017), "Prescription Opioids and Labor Market Pains: The Effect of Schedule II Opioids on Labor Force Participation and Unemployment," MPRA Paper No. 86586, October 7, 2017.

⁷⁶ Brent, David A., Kwan Hur, and Robert D. Gibbons (2019), "Association Between Parental Medical Claims for Opioid Prescriptions and Risk of Suicide Attempt by Their Children," *JAMA Psychiatry* Vol. 76, No. 9 (May): pp. 941-947.

⁷⁷ Powell, David, Abby Albert, and Rosalie L. Pacula (2019), "A Transitioning Epidemic: How the Opioid Crisis Is Driving the Rise in Hepatitis C," *Health Affairs* vol. 38, no. 2 (February): pp. 287-294.

⁷⁸ 2018 National Survey on Drug Use and Health Methodological Summary and Definitions, Section 4.2. <https://www.samhsa.gov/data/report/2018-methodological-summary-and-definitions>. Rx Use Disorder is defined as "Prescription Pain Reliever Use Disorder" by NSDUH. According to the 2018 NSDUH Annual Report, 97 percent

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social and interpersonal problems related to drug use, the frequency of hazardous use, legal problems related to use, the respondents' past attempts to quit or control use, the presence of withdrawal symptoms, and time spent using drugs. NSDUH data on Pain Reliever Use Disorder and HUD are available at the national and state level for 2002 through 2019. These data are not available for counties or for other sub-state regions. State-level data are reported in 2-year (through 2019) or 4-year (through 2018) intervals due to the relatively small size of state-specific samples. There was also a modification in the definition of pain reliever use disorder in 2015 that complicates comparison of this rate over time.

79. Exhibit 17 summarizes NSDUH estimates of opioid misuse and opioid-related disorders in 2006-09, the years preceding the onset of the increase in illicit mortality, and 2015-18, the most recent data available.⁷⁹ Exhibit 17 uses four-year averages to reduce the impact of year-to-year variations due to the relatively small size of the NSDUH sample. These data indicate that in 2006-09, an estimated 1.9 million people annually in the U.S. had OUD (0.77 percent of the U.S. population aged 12 and above).⁸⁰ This trend is consistent with the transition from prescription to illicit opioid use described above and reflects the fact that some of the increase in heroin use is itself causally related to prior shipments of prescription opioids.

or more of individuals who misused prescription pain relievers had misused a prescription opioid. NSDUH, "Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health," August 2019, p. 68.

⁷⁹ See: NSDUH, "2015 National Survey on Drug Use and Health - Summary of the Effects of the 2015 NSDUH Questionnaire Redesign: Implications for Data Users," June 2016, pp. 1, 4-6. The impact of this change appears to be modest. The national Pain Reliever OUD rate was 0.71 percent in 2014 and 0.77 percent in 2015. There was no change in the definition of HUD.

⁸⁰ Substance Abuse & Mental Health Data Archive's Public-use Data Analysis System (PDAS). (<https://pdas.samhsa.gov/#/>)

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Exhibit 17
Measures of U.S. Opioid-Related Disorder

	2006-2009	2015-2018	% Change
Heroin Use Disorder	0.12%	0.22%	84%
RX Use Disorder	0.69%	0.66%	-5%
Opioid Use Disorder	0.77%	0.80%	3%
Heroin Share of OUD	15.61%	27.73%	78%

Note: 4-year NSDUH averages used to reduce state-level variation due to small sample size.

2006-2009 Opioid UD defined as those with either Heroin or RX UD.

Source: NSDUH Restricted-use Data Analysis System.

80. It is widely recognized that NSDUH data understate the extent of OUD, Pain Reliever Use Disorder and HUD. For example, the NSDUH survey excludes homeless, incarcerated, and other institutionalized people who often have higher levels of drug use than the general population.⁸¹ In addition, survey respondents are generally hesitant to disclose use of illicit substances.⁸² A 2014 study from the RAND Corporation explains the difficulty of trying to measure the size of illicit drug activity:

⁸¹ See, National Academies of Sciences, Engineering and Medicine, "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," 2017 ("National Academies of Sciences, Engineering and Medicine (2017)"), p. 4-21. ("NSDUH [...] is a household-based sample that excludes institutionalized populations, homeless individuals, and others, and thus likely underestimates these outcomes.") See also, Report of The President's Commission on Combating Drug Addiction and the Opioid Crisis, November 1, 2017, available at https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-1-2017.pdf, ("President's Commission Opioid Report (2017)"), pp. 24, 60. ("Past 30 day users of heroin [...] is probably an underestimate because NSDUH surveys households and does not capture heroin users in homeless shelters or transient populations with no fixed address, and the incarcerated.") See also, Pitt, Allison L., Keith Humphreys and Margaret L. Brandeau. "Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic." *Am J Public Health*. 108 no. 10 (2018):1394-1400 ("Pitt et al. (2018)"), Supplement, p. S4. ("The National Survey on Drug Use and Health (NSDUH) tends to underreport opioid use disorder due to omission of some key populations (e.g., homeless, incarcerated) that are known to have high rates of illicit drug use [...]").

⁸² RAND Corporation, "What America's Users Spend on Illegal Drugs: 2000-2010," Prepared for U.S. Office of National Drug Control Policy, February 2014 (RAND (2014)), p. 11, available at https://obamawhitehouse.archives.gov/sites/default/files/ondcp/policy-and-research/ausid_results_report.pdf; National Academies of Sciences, Engineering and Medicine (2017); Keith Humphreys, "The federal government is systematically undercounting heroin users," *The Washington Post*, August 22, 2017, available at

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The difficulty is not conceptual; at root, it is just counting. The problem is largely with the data. That statement is in no way a criticism of those who design and administer data systems upon which we rely. Rather, it is an inevitable consequence of trying to measure sales of something sold in hidden markets or consumption behavior that is both illegal and dominated by a relatively small number of heavy users.⁸³

81. RAND estimates that the population of chronic users of heroin in the U.S., defined as those who used heroin four or more times in the previous month, was approximately 1.5 million people in 2010.⁸⁴ This is 2.5 times the NSDUH-based estimate of 600,000 for the same year.⁸⁵ However, even this comparison likely understates the extent of underreporting because the NSDUH data reflect estimates of both chronic and occasional users of heroin while the RAND study attempts to identify only chronic users.

82. Given the understatement of rates of OUD based on NSDUH, Pitt, Humphreys, and Brandeau implemented adjustments to the national rate of OUD in 2016 based on (i) the 2010 Rand study mentioned above; (ii) trends in HUD rates reported by NSDUH; and (iii) prescription opioid-related overdose deaths and assumptions about the likelihood of overdose for individuals with pain reliever use disorder.⁸⁶ Based on these adjustments, the authors estimate implies a national rate of OUD in 2016 of 1.41 percent, which is roughly 70 percent larger than the NSDUH reported rate.⁸⁷

https://www.washingtonpost.com/news/wonk/wp/2017/08/22/the-federal-government-is-systematically-under-counting-heroin-users/?utm_term=.b0343c34bc6a.

⁸³ RAND (2014), p. 7.

⁸⁴ See, RAND (2014), Table S.2. for the estimate of 1.5 million chronic heroin users. These figures are also cited in the President's Commission Opioid Report (2017), p. 60.

⁸⁵ President's Commission Opioid Report (2017), p. 60.

⁸⁶ Pitt et al. (2018). See also Pitt et al. (2018) Supplement, pp. S4-S5 and Table A.

⁸⁷ Pitt et al. estimate a rate of OUD in 2016 of 1.28 percent, consisting of a 0.77 percent rate of prescription OUD and a 0.51 percent rate of HUD. However, their estimate of HUD includes a haircut of 20 percent in order to exclude individuals with HUD who did not first have prescription OUD. The OUD rate of 1.41 percent mentioned above does not include this haircut ($1.41\% = 0.77\% + 0.51\%/80\%$).

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83. However, even the Pitt et al. estimate may understate the true population of individuals with OUD. For example, Barocas et al. (2018) estimate that 4.6 percent of Massachusetts adults suffered from OUD in 2015,⁸⁸ which is more than four times the NSDUH estimate of 1.0 percent.⁸⁹ The authors' estimate is based on an epidemiological capture-recapture analysis of seven de-identified Massachusetts health databases tracking various health outcomes.

2. Neonatal Abstinence Syndrome

84. NAS is a condition that may be diagnosed in a newborn that was exposed to drugs in the womb and requires hospitalization or treatment. NAS most often results from maternal use of opiates.⁹⁰ Data from the Healthcare Cost and Utilization Project (HCUP) report rates of NAS (expressed per 1,000 newborns delivered in a hospital or requiring hospitalization) from 2008 through 2018. Data for the U.S. are available for 2008-2017 and state-specific data are available for at least 40 states since 2008.

85. Exhibit 18 reports trends in NAS for the U.S. and shows that NAS increased by 230 percent between 2008 and 2017.

⁸⁸ Barocas, Joshua A., Laura F. White, Jianing Wang, Alexander Y. Walley, Marc R. LaRochelle, Dana Bernson, Thomas Land, Jake R. Morgan, Jeffrey H. Samet and Benjamin P. Linas. "Estimated Prevalence of Opioid Use Disorder in Massachusetts, 2011–2015: A Capture–Recapture Analysis." *AJPH Open Themed Research* Vol. 108 no. 12 (Dec 2018): 1675-1681.

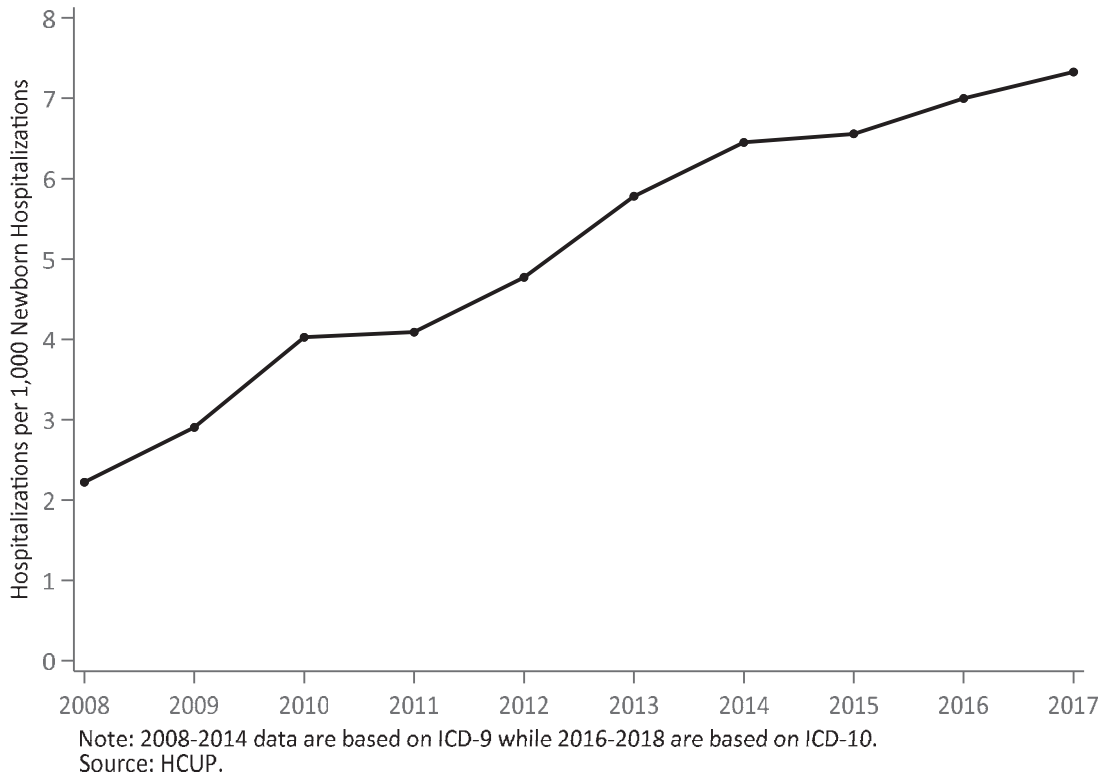
⁸⁹ Substance Abuse & Mental Health Data Archive's Restricted-use Data Analysis System (RDAS) (<https://rdas.samhsa.gov/#/>)

⁹⁰ Hudack, Mark L. and Rosemarie C. Tan. "Neonatal Drug Withdrawal." *Pediatrics* 129 (2) (February 2012). <https://doi.org/10.1542/peds.2011-3212>.

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Exhibit 18

National NAS Hospitalization Rate



3. Opioid-Related Hospital Visits

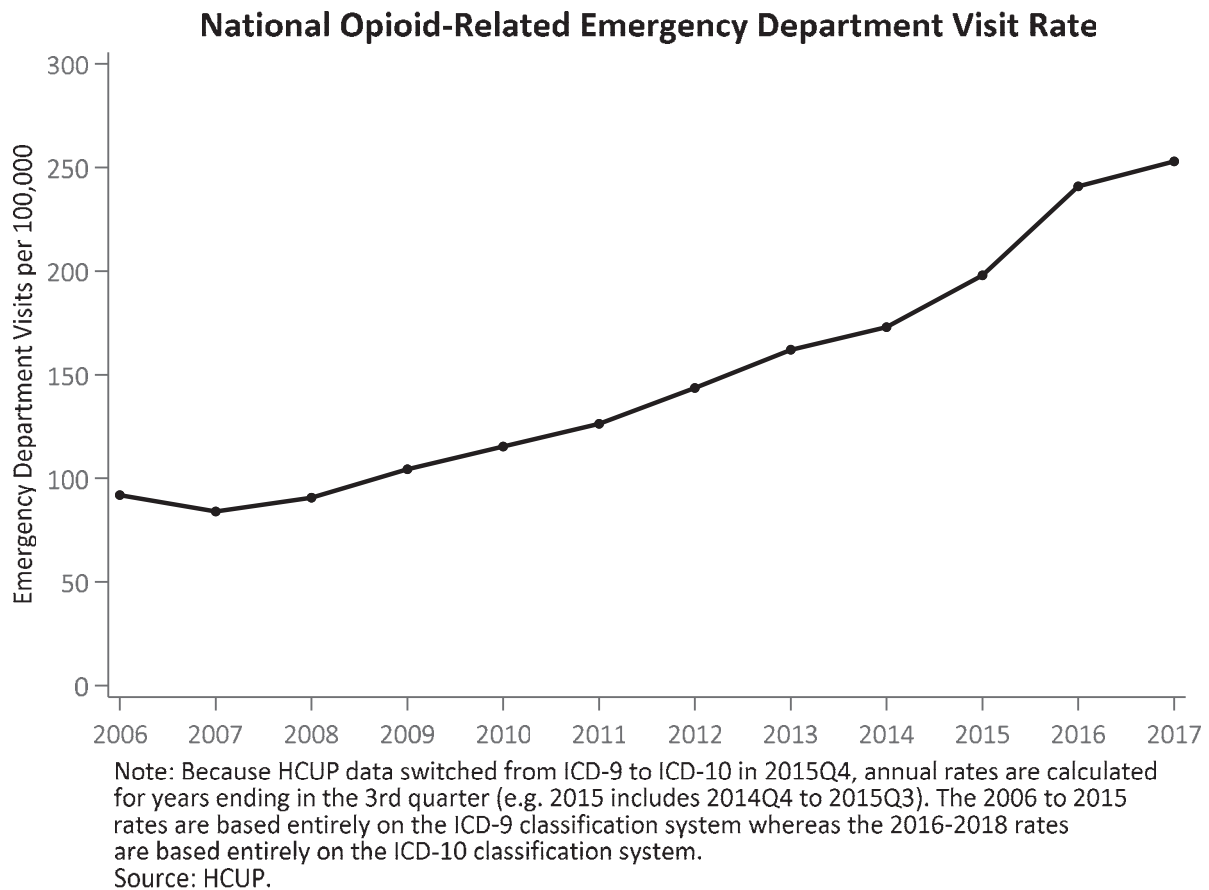
86. HCUP reports opioid-related inpatient admissions to hospitals and emergency department visits on a per capita basis beginning in 2005. Emergency department visits are defined as visits to an emergency room that do not result in an inpatient admission. Data are also reported on a state-specific basis starting in 2005. Interpretation of these data is complicated by a variety of factors including (i) an increase in the number of states reporting to HCUP over time; (ii) whether each state reports inpatient admissions, emergency department visits or both; and (iii) changes in the International Classification of Diseases (ICDs) in 2015 that affected the definition of opioid-related events.⁹¹

⁹¹ The data do not distinguish between events associated with prescription and illicit opioids.

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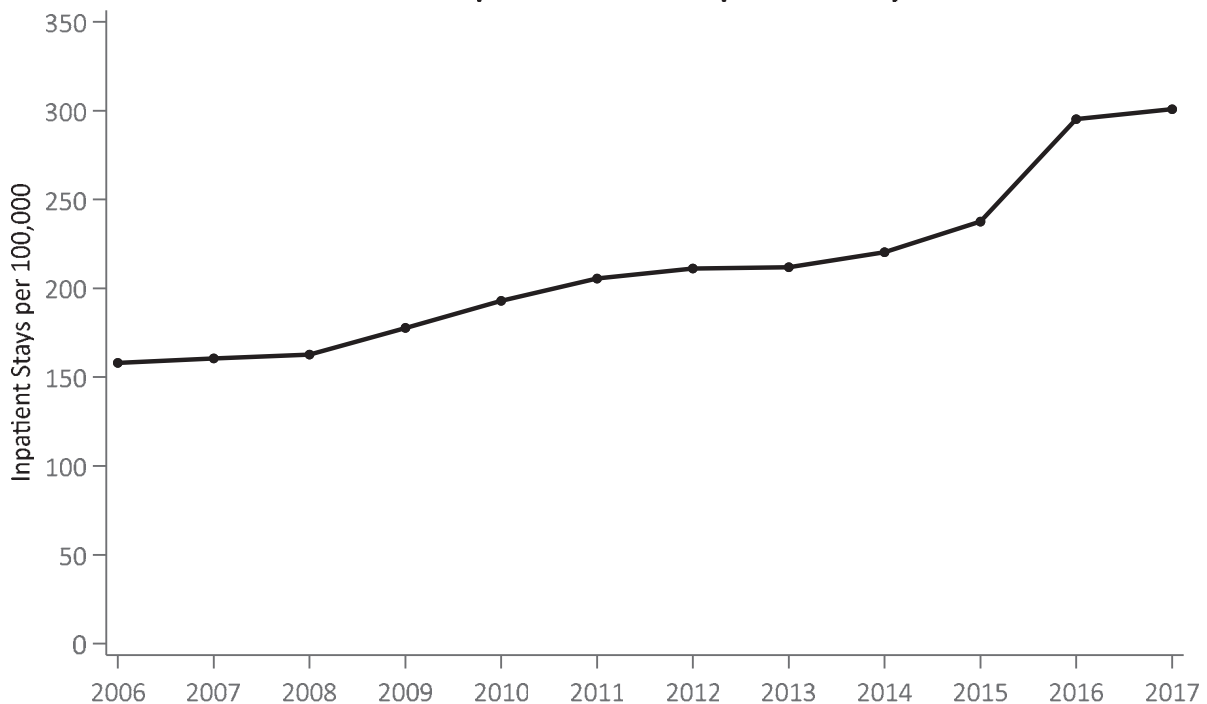
87. Exhibit 19 reports the rate of opioid-related emergency department for 2006-17 for the U.S. Over that period, such visits increased by 175 percent. Exhibit 20 reports similar data for opioid-related inpatient hospital stays for the same periods. Between 2006 and 2017, the peak year of inpatient stays, such stays increased by 90 percent for the U.S.

Exhibit 19



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Exhibit 20

National Opioid-Related Inpatient Stay Rate

Note: Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
Source: HCUP.

4. Foster Care

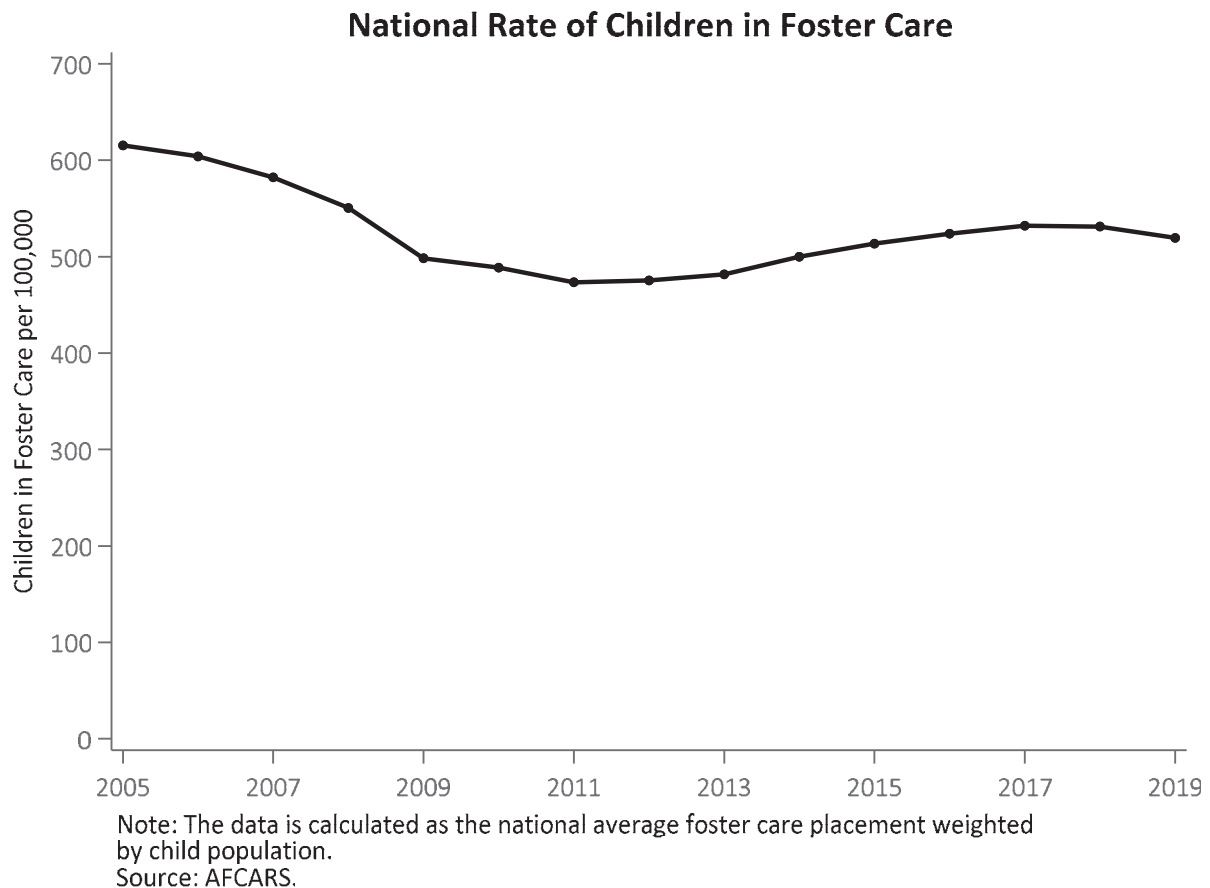
88. The opioid epidemic has resulted in increased caseloads for the child welfare system. A March 2018 study from the U.S. Department of Health and Human Services reports that the number of children in foster care rose by 10 percent between 2012 and 2016 and identified the opioid epidemic as a major contributing factor.⁹² A July 2019 study in the Journal of American Medicine: Pediatrics similarly found that foster care placements attributed to parental drug use increased substantially between 2000 and 2017, even as placements for

⁹² Radel, Laura, et al., "Substance Use, the Opioid Epidemic, and the Child Welfare System: Key Findings from a Mixed Methods Study," ASPE Research Brief, Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services, March 7, 2018.

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other reasons have fallen.⁹³ As shown in Exhibit 21, the increase in foster care placements starting in 2012 reversed a downward trend. The downward trend dated to the late 1990s and had resulted in a 30 percent reduction in foster care placements per 100,000 children.⁹⁴

Exhibit 21



IV. Opioid Related Mortality Was Caused by Shipments of Prescription Opioids

89. This section establishes that the opioid related mortality described above was caused by shipments of prescription opioids from an economic and statistical perspective.

⁹³ Meinhofer, Angelica, and Yohanis Anglero-Diaz, "Trends in Foster Care Entry Among Children Removed From Their Homes Because of Parental Drug Use, 2000 to 2017," JAMA Pediatrics 173, no. 9 (July 15, 2019): 881-883.

⁹⁴ See Table 11.3 of Green Book of House Ways and Means Committee, <https://greenbook-waysandmeans.house.gov/sites/greenbook.waysandmeans.house.gov/files/Figure%2011-3%20and%20Table%2011-3.pdf> (undated).

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When combined with estimates of the share of shipments that are related to defendants' misconduct, the analysis yields an estimate of the share of harms attributable to defendants' misconduct.

90. I first review what economists mean by "causation" and what I mean in concluding that the shipments of prescription opioids caused opioid-related harms. I then summarize the relationships between shipments and harms by comparing harms in states that received higher and lower levels of shipments. I finally undertake a series of statistical analyses that more formally establish these causal relationships.

A. How Economists and Other Empirical Researchers Evaluate Causation

1. Causation and Correlation

91. From an economic and statistical perspective, causation requires establishing "cause and effect" relationships. This involves comparing the actual state of the world with a "counterfactual" that reflects an estimate of the state of the world that would have existed in the absence of the cause. The counterfactual is often called the "but for" world since it reflects an estimate of what the world would have looked like in the absence of, or "but for," the alleged cause.

92. Establishing that prescription opioids caused increases over time in prescription and illicit opioid mortality requires more than just observing that both mortality and shipments increased over time. Two things can move in the same direction without having a causal relationship. For example, both opioid mortality and the use of the Internet have grown rapidly since the mid-1990s, but few would argue that the Internet "caused" opioid mortality (or vice-versa). While opioid mortality and use of the Internet are correlated – they move in similar ways over time or across areas – there is a higher bar for establishing a causal relationship.

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93. Establishing a causal relationship requires demonstrating that the “effect” was not the result of other factors that are not properly accounted for in the analysis. In the fields of economics and statistics (including health economics), research to identify and evaluate causal relationships is ubiquitous. Do shipments cause mortality? Does smoking cause cancer? Did the decline in housing prices cause the Great Recession? Does failure to wear masks cause the spread of Covid-19? There is no simple cookbook or checklist that can be invoked to establish causal relationships given the vast differences in the range of questions analyzed and differences in the scope of data available to address these questions – just as there is no cookbook that indicates how a judge should rule in a particular case. Rather, researchers use a variety of methods to distinguish causality from correlation.

94. At the same time, certain things are not required to establish a causal relationship. For example, establishing a causal relationship does not require that the “cause” explain 100 percent of the “effect.” More specifically, shipments of prescription opioids can cause an increase in opioid mortality even though other factors (including economic and demographic factors) also contribute to the effect. Moreover, establishing a causal relationship requires asking the right question. For example, establishing that shipments of prescription opioids cause increases in mortality does not require identifying the specific pill that resulted in an overdose, just as establishing a causal relationship between smoking and cancer does not require identifying the particular puff of a cigarette that triggered the growth of a cancerous cell. That narrow approach cannot necessarily be used to establish a causal relationship because multiple pills used over an extended period contribute to addiction and overdose deaths just as a history of smoking predisposes one to be more likely to develop cancer.

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95. Attempts to establish a causal relationship typically start with a theoretical basis to expect such a relationship. For example, there is no scientific basis to expect a causal relationship between Internet use and opioid mortality (after accounting for other factors that affect mortality). Thus, an analysis that established a statistically significant relationship between these factors for which there was no theoretical reason to expect a relationship would have to pass a very high hurdle. In the case of opioid use, there is a strong theoretical basis to expect a link between shipments of opioids and mortality. We typically know that a death is associated with an opioid overdose because it is identified as such on a death certificate.

96. As noted, a critical issue in establishing a causal relationship between shipments and harms is establishing that it was not something else correlated with shipments that led to the effect. In the case of opioids, some have argued that opioid mortality was driven by a broader set of social factors that led to increases in a variety of “deaths of despair,” including deaths from non-opioid drug use, alcohol-related liver disease, and suicide. This parallels closely the case of smoking and cancer, where tobacco companies argued for many decades that cancer was related to other consumption patterns correlated with smoking, but not smoking itself. Establishing that the estimated relationship between shipments of prescription opioids and opioid mortality is not due to other factors is an important focus of my analysis, just as establishing the relationship between cigarettes and cancer was an important part of the public health efforts directed against smoking.

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2. Economic and Statistical Factors in Establishing Causation

97. Methodologies for establishing causation have been the subject of extensive research and discussion in recent decades among economists and statisticians.⁹⁵ The general approach is succinctly summarized by Angrist and Krueger:

The first step is to specify a causal question, which we think of as comparing actual and counterfactual states. The next step is to devise a strategy that can, in principle, answer the question. A critical issue in this context is how the causal effect of interest is identified by the statistical analysis. In particular, why does the explanatory variable of interest vary when other variables are held constant? Who is implicitly being compared to whom? Does the source of variation used to identify the key parameters provide plausible "counterfactuals"? And can the identification strategy be tested in a situation in which the causal variable is not expected to have an effect? Finally, implementation of the empirical strategy requires appropriate data, and careful attention to the many measurement problems that are likely to arise along the way.⁹⁶

98. This literature stresses that there is no single approach to establishing causation that fits all circumstances. Angrist and Pischke's book-length guide to evaluating causal relationships discusses a range of empirical techniques that can be used including random assignment, regression, instrumental variables, regression discontinuity designs, and difference-in-differences. As they explain, the choice of the technique depends critically on the nature of the question addressed and availability of data.

99. No matter what approach is used, the fundamental concern in causal analysis remains the same – properly accounting for other factors that can contribute to opioid mortality. Further, as Angrist and Krueger stress, establishing a causal relationship requires

⁹⁵ See, for example: Angrist, Joshua D. and Alan B. Krueger, "Empirical Strategies in Labor Economics," Chapter 23 in *Handbook of Labor Economics* Vol. 3, Ed. O. Ashenfelter and D. Card, Elsevier Science, 1999. ("Angrist and Krueger"), pp. 1277-1366; Athey, Susan and Guido W. Imbens, "The State of Applied Econometrics: Causality and Policy Evaluation," J. Econ Perspectives (Spring 2017) ("Athey and Imbens") and Angrist, Joshua and Jörn-Steffen Pischke, *Mastering Metrics: The Path from Cause to Effect* Princeton: Princeton University Press, 2013 ("Angrist and Pischke (2013)").

⁹⁶ Angrist and Krueger, pp. 1345-1355.

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understanding the source of variation in the “causal” variable. Here, if variation in shipments of prescription opioids across different areas is itself the consequence of prior levels of opioid mortality in an area, then the analysis cannot be said to establish a causal relationship. But there is no evidence to suggest that this circumstance arises here.

100. As this discussion suggests, establishing a causal relationship is typically a multi-step process requiring both a primary analysis (here, analyzing the relationship between shipments of prescription opioids and mortality) as well as supplemental analyses that investigate the reliability of the results. Athey and Imbens stress two types of supplemental analysis: (i) evaluation of the sensitivity of the results to changes in statistical specification, such as including or excluding different types of control variables and/or testing the model on different data sets; and (ii) “placebo” tests to determine whether the analysis establishes a statistically significant relationship in circumstances in which there is no theoretical basis to expect a relationship. If such a relationship is found where none is expected, it can call into question whether the “primary” model identifies a causal relationship.

101. My analysis undertakes several supplemental analyses to confirm the causal relationship between shipments of prescription opioids on prescription opioid mortality and illicit opioid mortality. This analysis makes use of rich data sources that identify both historical shipments of opioids and opioid mortality for detailed geographic areas over a period of more than 20 years, including years before the opioid epidemic.

- I use regression analysis based on state-level data to establish statistically significant relationships between prescription and illicit opioid mortality and shipments to different areas that control for a wide range of factors that might affect opioid mortality.

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- I use regression analysis to identify discontinuities in trends in prescription and illicit opioid mortality to establish that policy responses to the prescription opioid crisis caused the illicit opioid crisis.
- I investigate the sensitivity of the results to changes in statistical specification, investigate the sources of variations in shipments across geographic areas, and perform various placebo tests in evaluating the reliability of my results, including analysis of the impact of shipments on non-opioid deaths of despair.

102. I also analyze the relationship between shipments of prescription opioids and a variety of other opioid-related harms, including OUD, HUD, neonatal abstinence syndrome, opioid-related emergency department visits and inpatient hospital admissions, and foster care placements. Data on these harms are available for limited time periods and with less geographic specificity than mortality data. While my analysis establishes systematic relationships between shipments and these harms, the strength of these relationships is not as strong as that established for the link between shipments and mortality. This is largely due to data limitations: data on harms other than mortality are measured with more error and typically for a shorter period of time. Nonetheless, these results, together with those relating to mortality, provide additional evidence in support of the conclusion that there is a causal relationship between shipments of prescription opioids and the harms associated with the opioid crisis.

103. The causal relationship between shipments of prescription opioids and opioid-related harms implies that, all else equal, areas that received greater levels of shipments systematically experienced greater levels of harms. Note that this analysis does not imply that areas that received relatively fewer shipments were not affected by those shipments. Rather,

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my analysis shows that shipments were elevated in all areas due to defendants' misconduct so all areas experienced opioid-related harms caused by defendants.

104. To the extent that shipments were elevated by defendants' misrepresentations and/or failure to monitor and prevent diversion – topics addressed by other experts – defendants' misconduct can be said to have caused an increase in opioid-related harms. Harms caused by defendants' misconduct can be then said to have occurred in all areas in which defendants' misconduct resulted in elevated shipments.

B. Comparison of Mortality Trends in States with High and Low Levels Shipments of Prescription Opioids

105. The relationship between shipments and opioid mortality is readily observed in simple comparisons of trends in opioid mortality in states that received high and low levels of per capita shipments of prescription opioids between 1997 and 2010. My analysis focuses on aggregate shipments over this period because the changes in the prescription opioid marketplace after 2010, including legal and regulatory actions and the reformulation of OxyContin altered the relationship between shipments and prescription mortality, and because the shipments over this period set in motion the increase in illicit mortality after 2010. My approach also considers the fact that shipments of opioids in a single period can have long-lasting effects beyond the period in which they were shipped.

106. In summarizing these trends, I compare changes in mortality in the states that account for 25 percent of the population that received the highest level of per capita shipments over this period and the 25 percent of these states that received the lowest level of such shipments. As a point of comparison, between 1997 and 2010, per capita shipments in the high-shipment states was 1.90 MME per capita per day, nearly double the rate of 0.98 in low shipment states.

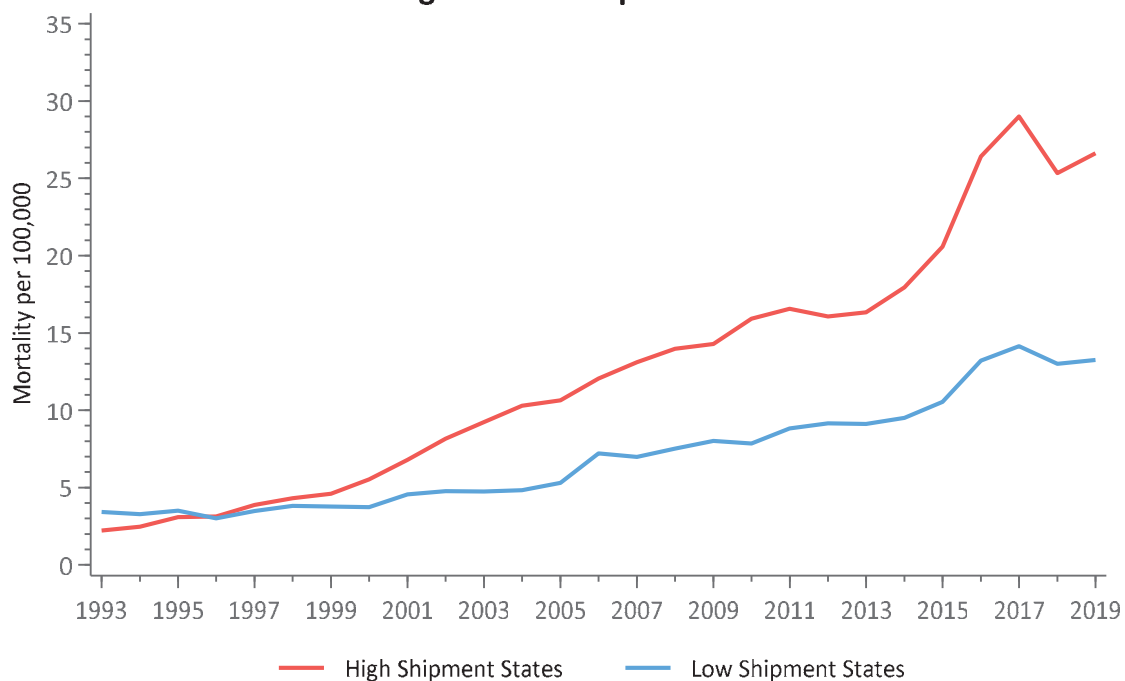
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107. Exhibits 22-24 show that high shipment states experienced greater growth in opioid mortality than did low shipment states for both prescription and illicit opioid mortality.

- Exhibit 22 establishes that opioid mortality in high shipment states grew much more rapidly than in low-shipment states between 1993 and 2019 even though they started at approximately the same level in 1993. Between 1993 and 2017, the year of peak opioid mortality, total opioid mortality rates in high shipment states increased by 1,212 percent compared to 312 percent in low shipment states.

Exhibit 22

Total Opioid Mortality Rate: 1993-2019
High vs. Low Shipment States



Source: NCHS Mortality Data and Census Data.

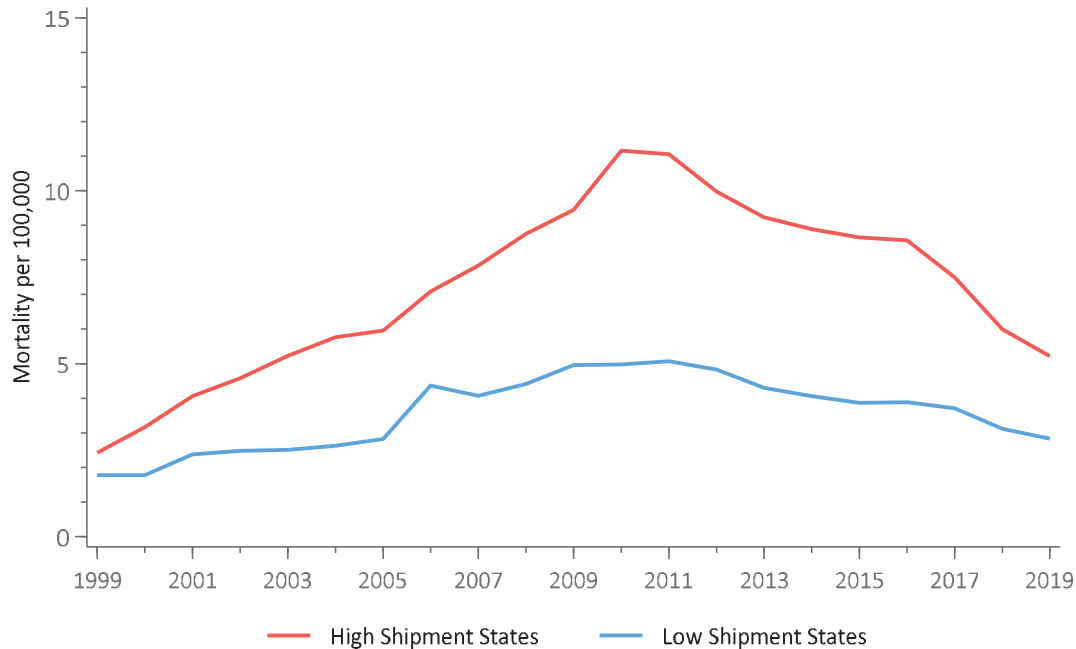
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- Exhibit 23 compares the growth in prescription opioid mortality since 1999 in high and low shipment states. As discussed above, available data identify mortality by opioid type starting in 1999. Between 1999 and 2011, prescription opioid mortality grew 356 percent in high shipment states compared to 185 percent in low shipment states. As also discussed above, prescription opioid mortality has fallen since 2011 in both high and low shipment states. In high shipment states, per capita shipments fell by 59 percent between 2010 and 2019 and prescription opioid mortality fell by 53 percent. In low-shipment states, per capita shipments fell by 49 percent over this period and prescription opioid mortality fell by 43 percent. Nevertheless, in 2019, prescription opioid mortality rates in high shipment states remained 84 percent above levels in low shipment states.

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Exhibit 23

Prescription Opioid Mortality Rate: 1999-2019
High vs. Low Shipment States



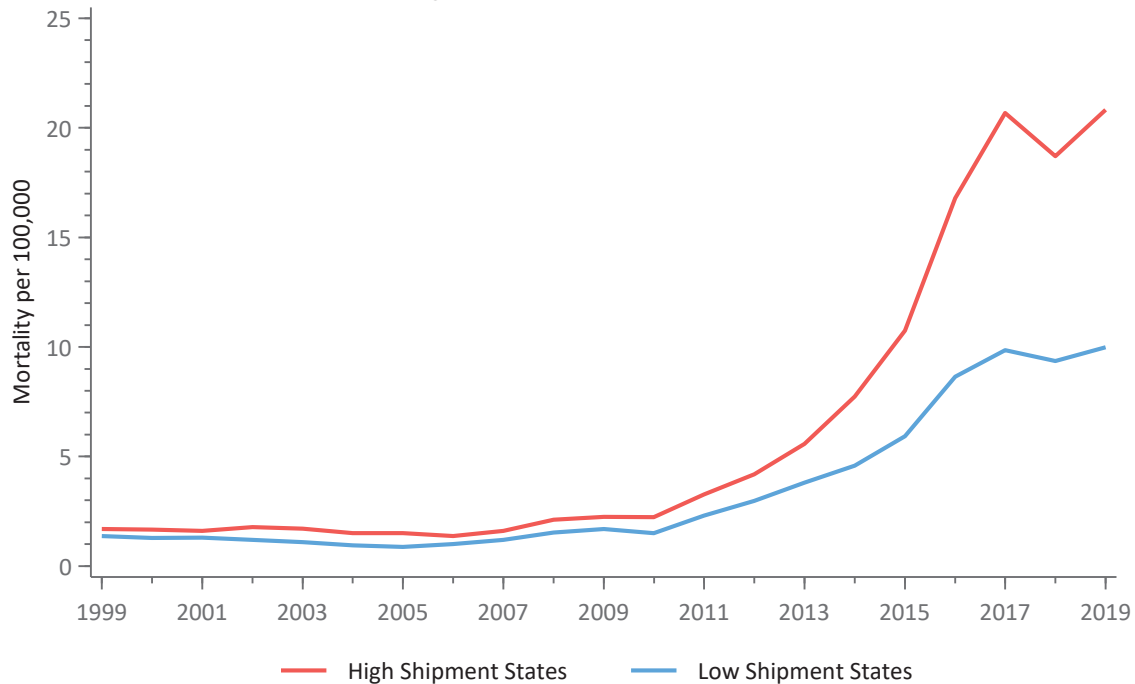
Source: NCHS Mortality Data and Census Data.

- Exhibit 24 compares the growth in illicit mortality since 1999 in high and low shipment states. Prior to 2010, illicit mortality was roughly comparable in high and low shipment states and followed generally similar trends, declining modestly in both areas between 1999 and 2006 and increasing modestly in both areas between 2006 and 2010. In 1999, illicit opioid mortality was 24 percent higher in high-shipment states compared to low-shipment states, with the difference growing to 49 percent in 2010. Between 2010 and the peak year of 2017, illicit mortality grew 826 percent in high-shipment states compared to 559 percent in low-shipment states. In 2017, illicit mortality rates in high shipment states were roughly double those in low-shipment states.

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Exhibit 24

**Illicit Opioid Mortality Rate: 1999-2019
High vs. Low Shipment States**



Source: NCHS Mortality Data and Census Data.

108. All these patterns are consistent with the hypothesis that the growth in mortality from both prescription and illicit opioids is the direct consequence of shipments of prescription opioids. This helps to demonstrate that defendants' misconduct is causally related to opioid-related harms in all areas. The following section presents a more comprehensive statistical analysis to help establish the causal relationship between shipments and opioid mortality.

C. Regression Framework for Evaluating the Relationship between Shipments and Mortality

109. While informative, the comparisons of mortality trends in high and low shipment states above do not control for factors that may affect opioid-related mortality other than the level of shipments. To control for such factors, I use regression analysis based on state-level

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data to estimate the relationship between the increase in opioid-related mortality and per capita shipments of prescription opioids to the state. The regression model includes variables that control for differences in the economic and demographic factors that may affect opioid mortality in a state. The regressions are discussed in more detail below and results are presented in the appendices identified below.

110. The regression analysis yields an estimate of the magnitude and statistical significance of the relationship between shipments and mortality, controlling for a variety of economic and demographic factors that may affect opioid mortality in a state. Regression analysis is a reliable and commonly used method to analyze the relationship between economic variables and is widely applied in economics and other social sciences and in expert analysis in litigation.⁹⁷ The construction of the data used in this analysis is described in Appendix 3.

111. My analysis applies the “long difference” methodology which measures the change in an outcome variable – in this case, opioid-related mortality – over a long period of time and estimates the relationship between that change in the outcome and observable factors – in this case, prescription opioid shipments as well as economic and demographic factors. Economists have applied the long difference methodology to evaluate, among other things, the impact of expanded trade with China on employment by industry and geography and the effect of crime on property values.⁹⁸ I regularly use “long difference” models in my

⁹⁷ See, for example: Rubinfeld, Daniel L. “Reference Manual on Multiple Regression,” *Reference Manual on Scientific Evidence* 3rd. Ed. Federal Judicial Center, National Academies Press (2011): 303-358.

⁹⁸ For example, see: Autor, David H., David Dorn, and Gordon H. Hanson. “The China Syndrome: Local Labor Market Effects of Import Competition in the United States.” *American Economic Review* 103 (2013): 2121–2168; Autor, David H., David Dorn, and Gordon H. Hanson. “The China Shock: Learning from Labor Market Adjustment to Large Changes in Trade.” *Annual Review of Economics* 8 (October 2016): 205-220; Ruhm (2018); Devin G. Pope and Pope, Jaren C. “Crime and Property Value: Evidence from the 1990s Crime Drop.” *Regional Science and Urban Economics* 42 (2012): 177-188.

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research, including to analyze changes in suicide over time and in valuing improvements in medical services, among other areas.⁹⁹

112. The long difference methodology is appropriate here because it accounts for the fact that the relationship between prescription opioid shipments and opioid mortality is unlikely to be instantaneous, due to the long-term effects of addiction. As noted, the model controls for a variety of factors other than shipments that potentially affect opioid mortality. One variable included in the model is the area's opioid mortality rate in the starting period, which captures potential mean reversion which occurs when areas with lower initial mortality have larger mortality increases simply because they are catching up to otherwise comparable areas (or vice-versa).

113. The analysis also includes variables that account for long-term changes in economic conditions that have been identified as affecting "Deaths of Despair."¹⁰⁰ These include factors that approximate the impact of changes in economic opportunity on opioid mortality over the relevant sample periods. The economic variables included are the change in the prime age male employment to population ratio, the change in median household income, and the change in the state's population between the base and post periods. Demographic variables in the model include the change in the share of the population that is white and the change in the share of the population with less than a high school degree. These variables

⁹⁹ Cutler, David M., Edward L. Glaeser and Karen E. Norberg. "Explaining the Rise in Youth Suicide," in Jonathan Gruber, ed., *Risky Behavior Among Youths: An Economic Analysis*, Chicago: University of Chicago Press, 2001: 219-269 (Cutler et al (2001)); Cutler, David M., Allison B. Rosen and Sandeep Vijan. "Value of Medical Innovation in the United States: 1960-2000." *New England Journal of Medicine* 355:(2006): 920-927.

¹⁰⁰ See, e.g., Case, Anne and Sir Angus Deaton. "Mortality and Morbidity in the 21st Century." *Brookings Paper on Economic Activity*. (Spring 2017): 397-443 (Case and Deaton (2017)); Case, Anne and Angus Deaton, "Rising Morbidity and Mortality In Midlife among White Non-Hispanic Americans in the 21st Century." *Proceedings of the National Academy of Sciences* 112(2015): 15078-83 (Case and Deaton (2015)). Case and Deaton define "Deaths of Despair" to include deaths due to drug overdoses, suicides, and alcohol-related liver diseases.

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correspond to the set of factors which researchers have posited could explain the large increases in opioid-related mortality and other “Deaths of Despair.”¹⁰¹

114. The regression yields an estimate of the average relationship between aggregate per capita shipments to an area and changes in opioid mortality over a specified time period. I estimate a series of regression models that evaluate the relationship between shipments and opioid mortality of various types and over different periods of time. If the relationship between shipments and mortality changes due, for example, to the emergence of the illicit opioid crisis, regression analysis can be used to evaluate whether a “structural change” in the relationship has occurred.

115. Available data are subject to various limitations that have the likely effect of yielding an estimate that *understates* the true relationship between prescription opioids and opioid mortality. For example, the MCODE data reflect deaths of *residents* of an area, they do not reflect deaths that *occurred* in the area, which includes individuals that reside elsewhere. Thus, mortality is likely to be undercounted in an area if areas with high shipments attract users of illicit opioids that result in overdose deaths.

116. My analysis relies on data on aggregate levels of MMEs shipped to a state. Available data do not permit the evaluation of specific characteristics of prescription opioids that may affect misuse and mortality such as average dosage size and average duration of prescriptions. By necessity, the analysis treats all MMEs as equal although MMEs in high dosage pills or long-duration prescriptions may have a stronger relationship to mortality than

¹⁰¹ Case and Deaton (2017); Ruhm (2018).

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those in low-dosage pills and shorter-duration prescriptions. Limitations of this type typically result in regression estimates that underestimate true economic relationships.¹⁰²

117. The regression analyses yield estimates of the impact of shipments on opioid mortality rates which is evaluated as the difference between actual rates and rates expected if shipments had remained at 1997 levels.

D. Regression Estimates of the Impact of Shipments on Opioid Mortality: 1993-2010

118. This section details the results of analysis based on the regression framework described in the preceding section for 1993 through 2010, immediately prior to the start of the illicit opioid crisis. The results are summarized in

119. Exhibit 25 below. The complete output from these regressions is presented in Appendix 6. I address the relationship between shipments of prescription opioids and the illicit crisis immediately after.

- Model 1 relates per capita shipments between 1997-2010 and changes in total opioid mortality between 1993-95 and 2009-10.¹⁰³ The analysis yields a large positive and statistically significant relationship between these variables. The results based on the state level data indicate that had shipments remained at levels observed in 1997 then the opioid mortality rate in 2010 would have been 3.26 per 100,000 instead of the actual rate of 11.86. This means that shipments of

¹⁰² See, for example, Wooldridge, Jeffrey M. *Econometric analysis of cross section and panel data*. Cambridge, Massachusetts: MIT press, 2010, pp. 80-81 for a discussion of errors in variables.

¹⁰³ To reduce the possible influence of random variation in state-level mortality data, I evaluate the change in average mortality for 1993-95 and 2009-10. The reported results are based on unweighted regressions and robust standard errors are reported.

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prescription opioids raised the national mortality rate by approximately 263 percent relative to the level otherwise expected.

- Model 2 relates per capita shipments of prescription opioids and the change in prescription opioid mortality between 1999-2000 and 2009-10.¹⁰⁴ The results again identify a large positive and highly statistically significant relationship between these variables. These results indicate that if prescription opioid shipments remained at levels observed in 1997 then the prescription opioid mortality rate in the U.S. in 2010 would have been 2.71 per 100,000 instead of the actual rate of 7.99. This means that shipments of prescription opioids raised the national prescription opioid mortality rate by approximately 195 percent relative to the level otherwise expected.
- Model 3 reflects the regression estimate of the relationship between shipments of prescription opioids and the change in illicit opioid mortality rate between 1999-2000 and 2009-10. These results establish a positive but statistically insignificant relationship between these variables over this period. While the rapid growth in illicit opioid mortality did not start on a national basis until after implementation of responses to the prescription opioid crisis in 2010, over the prior decade it had been increasing in some areas but decreasing in others. For example, as discussed above, prescription opioid shipments can lead to illicit opioid mortality both before and after reforms to the prescription opioid marketplace during Phase 2 of the crisis. These regression results suggest that shipments of prescription opioids

¹⁰⁴ The analysis compares the change in average prescription opioid mortality rates in 1999-2000 and 2009-10. Prescription opioids in this analysis include fentanyl.

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in a state were associated with greater growth in illicit opioid mortality before 2010.

Exhibit 25

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Change in Opioid-Related Mortality through 2010

Model	Mortality Type	Base Period	Post Period	Coefficient on Shipments				Implied Impact of Increase in Shipments on 2009-2010 Mortality Rate		
				Beta	Std. Err.	T-Stat.	P-Value	Actual Mortality Rate	Implied But-For Mortality Rate	
									Mortality Rate	Percent Elevation
1	Any Opioid	1993-1995	2009-2010	8.57	1.48	5.80	0.00	11.86	3.26	263.3%
2	Prescription Opioids	1999-2000	2009-2010	5.27	1.18	4.46	0.00	7.99	2.71	195.0%
3	Illicit Opioids	1999-2000	2009-2010	0.30	0.35	0.85	0.40	1.58	1.28	23.4%

Notes:

Robust standard errors.

Control variables for all regressions: Shipments per capita per day (average 1997-2010); base period non-mortality harm rate; change in percent of population white; change in median household income; change in percent less than high school; change in prime male employment to population; percentage change in total population.

But-For mortality based on assumption that shipments remain at 1997 levels.

Excludes DC and Puerto Rico.

E. Opioid Shipments and the Growth of Illicit Mortality after 2010

120. This section establishes that the illicit crisis that began after 2010 was caused by the shipments of prescription opioids in earlier years. This section first identifies statistically significant “structural changes” reflecting both a decline in prescription opioid mortality rates and rapid increases in illicit mortality rates both starting in 2010. I also show that states with high shipments experienced a significantly more rapid escalation in illicit opioid mortality than low shipment states. This section then uses state-level regression analysis to establish: (i) that increases in illicit mortality after 2010 are directly related to shipments in prior years; and (ii) that increases in total opioid mortality between 1993-95 and 2018-19 are directly related to shipments.

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1. Structural changes in opioid mortality trends

121. As discussed above, the market for prescription opioids changed dramatically in and around 2010 due to increased regulatory oversight, the release of the abuse deterrent form of OxyContin, and the reversal of 15 years of increasing shipments. These market changes decreased the supply of prescription opioids and increased the demand for illicit opioids among dependent individuals. This section identifies structural changes in prior trends in opioid mortality rates that coincide with reforms in the opioid marketplace. These results are an element in establishing the causal relationship between the emergence of the illicit opioid crisis and shipments of prescription opioids in prior years.

122. The analysis is based on regression analysis of monthly time series data on prescription opioid mortality between 1999 and 2019. Structural changes in trends are identified by estimating a series of regression models that permits analysis of different trends before and after a range of different “break points.” For each potential break point, a regression is run that yields an estimate of the change in trends before and after the specified break as well as a test of whether the change in the trend is statistically significant. The date of the structural change is determined based on the break point that yields the most highly statistically significant difference between the before/after trends.¹⁰⁵

¹⁰⁵ The test evaluates the month in which the level and trend is mostly likely to have shifted based on the largest F-statistic from a joint test of these parameters before and after the alternative break points. See, Chow, Gregory C. "Tests of equality between sets of coefficients in two linear regressions." *Econometrica: Journal of the Econometric Society* 28 (1960): 591-605; Quandt, Richard E. "Tests of the hypothesis that a linear regression system obeys two separate regimes." *Journal of the American statistical Association* 55 (1960): 324-330; Fisher, Franklin M. "Tests of equality between sets of coefficients in two linear regressions: An expository note." *Econometrica: Journal of the Econometric Society* 28 (1970): 361-366. An F-statistic is used in econometrics to test whether the values across two groups differ from each other. The largest F-statistic identifies the month associated with the largest difference in the trends (growth rates) for heroin mortality between the two periods.

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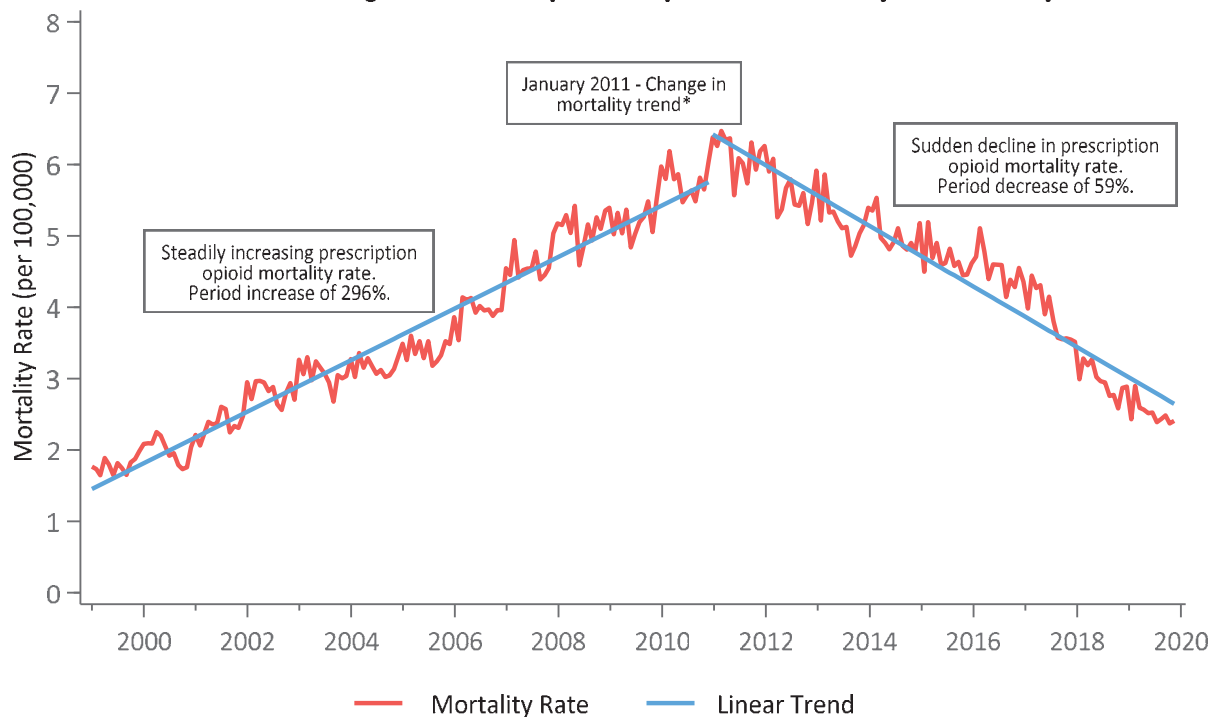
123. Exhibits 26-28 establish that structural changes in prescription opioid and illicit opioid mortality trends for the U.S. occurred late in 2010 or early in 2011.¹⁰⁶ These structural changes are highly statistically significant.

- Exhibit 26 establishes that the structural change in the prescription opioid mortality trend occurred in or around January 2011. The analysis is based on deaths in which prescription opioids (but no illicit opioids) are identified in death data. Prescription opioid mortality had been rising steadily through the 2000s and the trend then reversed, with January 2011 providing the best estimate of the timing of the reversal.

¹⁰⁶ Structural break analyses for illicit opioid mortality trends are also reported in Evans, William N., Ethan Lieber, Patrick Power. "How the Reformulation of Oxycontin Ignited the Heroin Epidemic." *Review of Economics and Statistics* 101 no. 1 (2019) and Ruhm, Christopher J., "Drivers of the Fatal Drug Epidemic," *Journal of Health Economics* vol. 64 (2019). Both studies reach conclusions similar to my own.

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Exhibit 26

Structural Change in Prescription Opioid Mortality in January 2011

Notes: Prescription Opioids exclude fentanyl.

* Statistically identified as month of change in mortality trend. F-statistic of test that parameters for shift in intercept and slope are jointly zero is statistically significant with a p-value of 0.0000. Differences in intercept and slope are statistically significant at probability <0.01 and have estimates of 22.68 (p-value 0.0000) and -0.07 (p-value 0.0000), respectively.

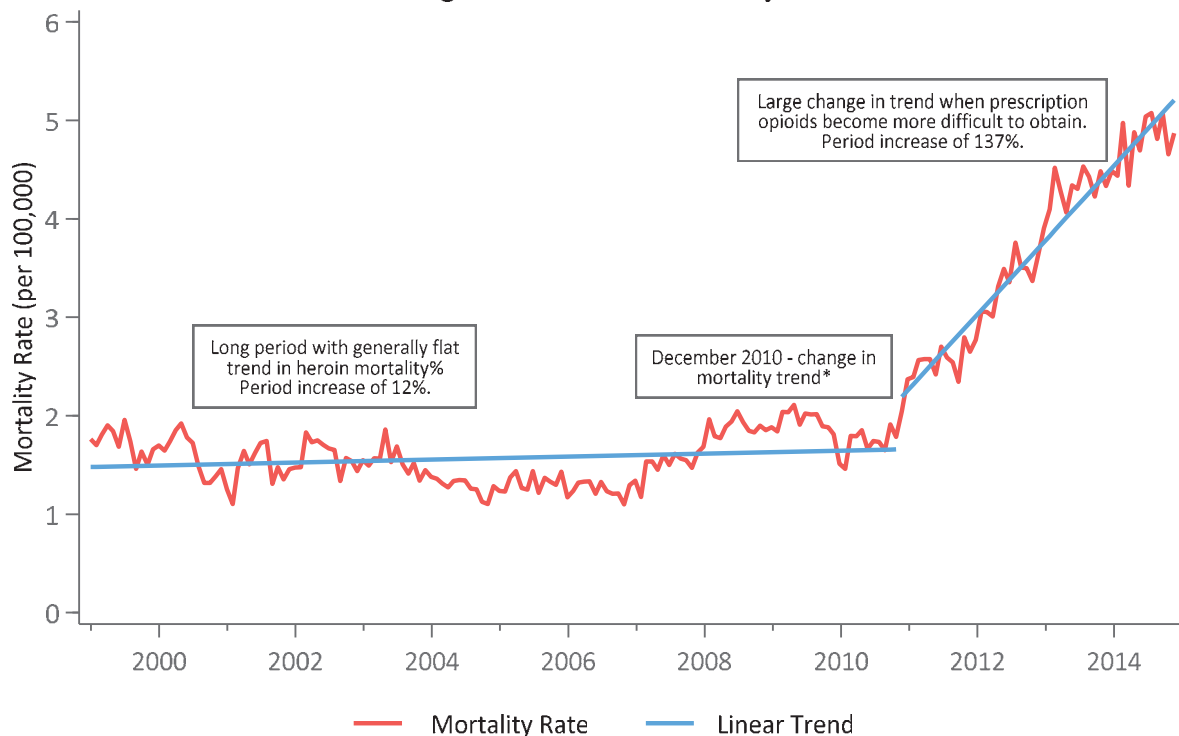
Source: NCHS Mortality Data.

- Exhibit 27 establishes that the structural change in trends in mortality involving heroin occurred in or around December 2010. Prior to that date, heroin mortality rates followed no material systematic trend since 1999 but then started a rapid increase through 2014. The analysis excludes later years because both heroin and fentanyl are often identified as causes of death for many opioid-related overdoses after 2014, when illicit fentanyl became more widely available. The timing of this structural change coincides with the changes in the prescription opioid marketplace discussed above.

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Exhibit 27

Structural Change in Heroin Mortality in December 2010



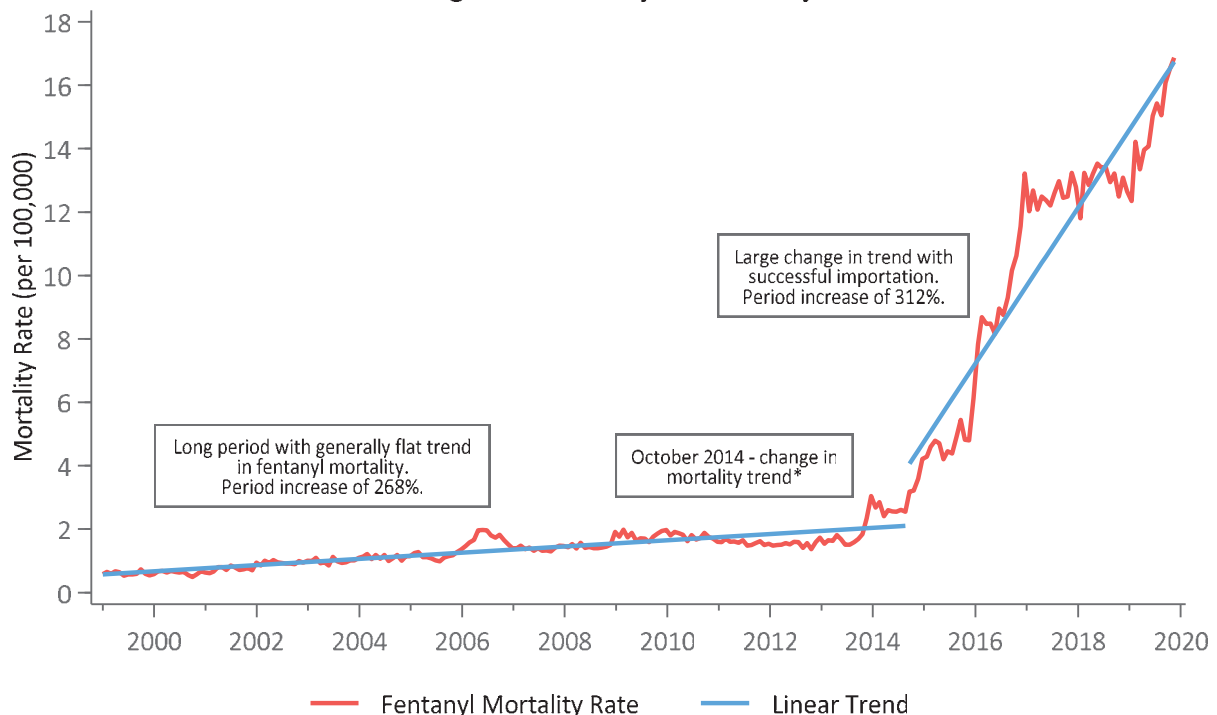
Note: * Statistically identified as month of change in mortality trend. F-statistic of test that parameters for shift in intercept and slope are jointly zero is statistically significant with a p-value of 0.0000. Differences in intercept and slope are statistically significant at probability <0.01 and have estimates of -20.12 (p-value 0.0000) and 0.06 (p-value 0.0000), respectively.
Source: NCHS Mortality Data.

- Exhibit 28 establishes that a structural change in fentanyl-related mortality trends occurred on or around October 2014. The analysis is based on deaths in which fentanyl is identified as a cause of death between 1999 and 2019. Fentanyl-related mortality followed a slow upward trend prior to April 2014 and then accelerated rapidly. The estimated timing of the structural change coincides with recognition that illicit imports of fentanyl were entering into the US.¹⁰⁷

¹⁰⁷ U.S. Department of Justice Drug Enforcement Administration, "2014 National Drug Threat Assessment," available at <https://www.dea.gov/documents/2014/11/01/2014-national-drug-threat-assessment>, pp. 1, 15; See also CDC Health Advisory, "Increases in Fentanyl Drug Confiscations and Fentanyl-related Overdose Fatalities," October 25, 2015, available at <https://emergency.cdc.gov/han/han00384.asp>.

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Exhibit 28

Structural Change in Fentanyl Mortality in October 2014

Notes: * Statistically identified as month of change in mortality trend. F-statistic of test that parameters for shift in intercept and slope are jointly zero is statistically significant with a p-value of 0.0000. Differences in intercept and slope are statistically significant at probability <0.01 and have estimates of -73.00 (p-value 0.0000) and 0.20 (p-value 0.0000), respectively. Fentanyl mortality in this figure includes mortality associated with both Fentanyl and Heroin.
Source: NCHS Mortality Data.

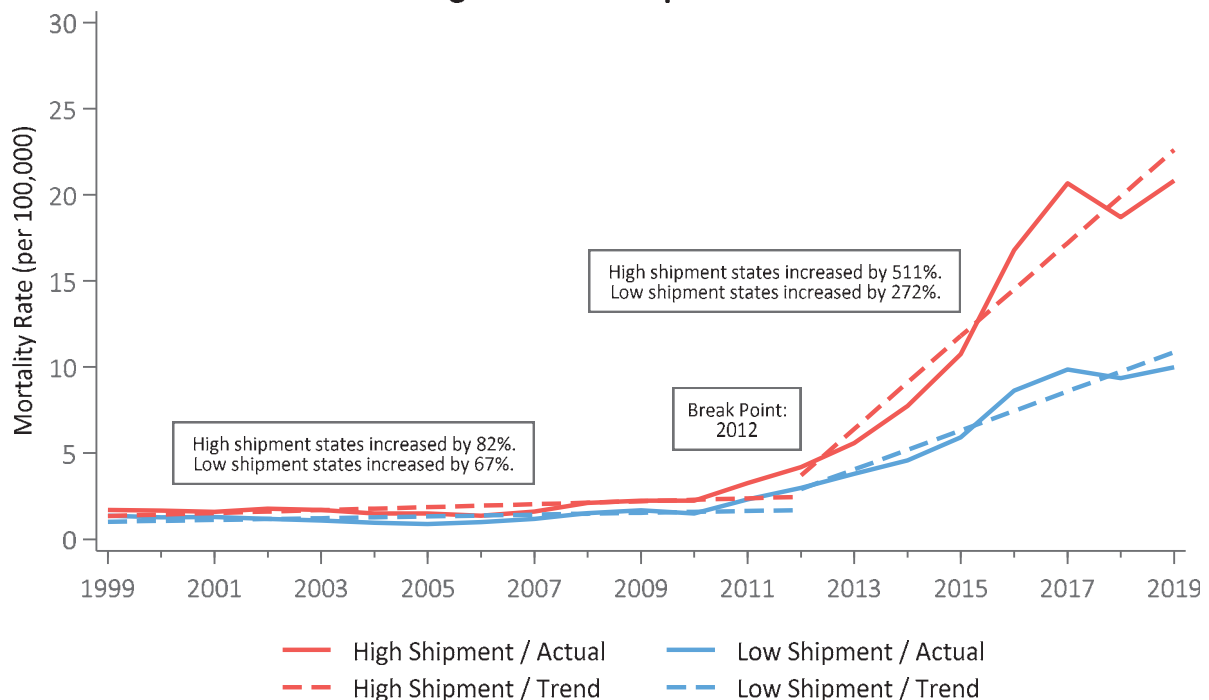
- Exhibit 29 identifies structural changes for illicit opioid mortality (involving either fentanyl or heroin) separately for high and low shipment states. This analysis is based on annual instead of monthly data because state-level mortality data are not available monthly. The analysis establishes that there was a structural change in illicit opioid mortality in both sets of states in 2012, but that high shipment states experienced a significantly greater increase in illicit mortality than low-shipment states. While the underlying trends in illicit mortality in high and low shipment states begin to diverge around 2010, the break point here is somewhat later than above (2012 vs. 2010) due to widening of the gap after illicit fentanyl became more widely available in Phase 3. The analysis also establishes that the

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difference in the estimated trends in illicit mortality in the post-2010 period for high and low shipment states is statistically significant.

Exhibit 29

Structural Changes in Illicit Opioid Mortality High vs. Low Shipment States



Note: F-statistic of test that difference in intercept parameters and difference in slope parameters are jointly zero is statistically significant. Difference in change in slope between high and low shipment areas is 1.533 and difference in change in level is 21.443; test of joint significance has a p-value of 0.000.
Source: NCHS Mortality Data and ARCOS

124. Additional analysis demonstrates that the increase in opioid-related mortality between 2010 and 2019 cannot be explained by changes in economic and demographic factors. This is established by analyzing the demographic and economic factors associated with illicit mortality across states prior to the illicit crisis and then projecting how illicit mortality rates would have changed based on changes in these factors alone. This “indirect” approach is based on a cross-section regression using state-level data in 2009-2010 which relates a state’s opioid mortality rate in that period to the following factors: the percent of population that is male,

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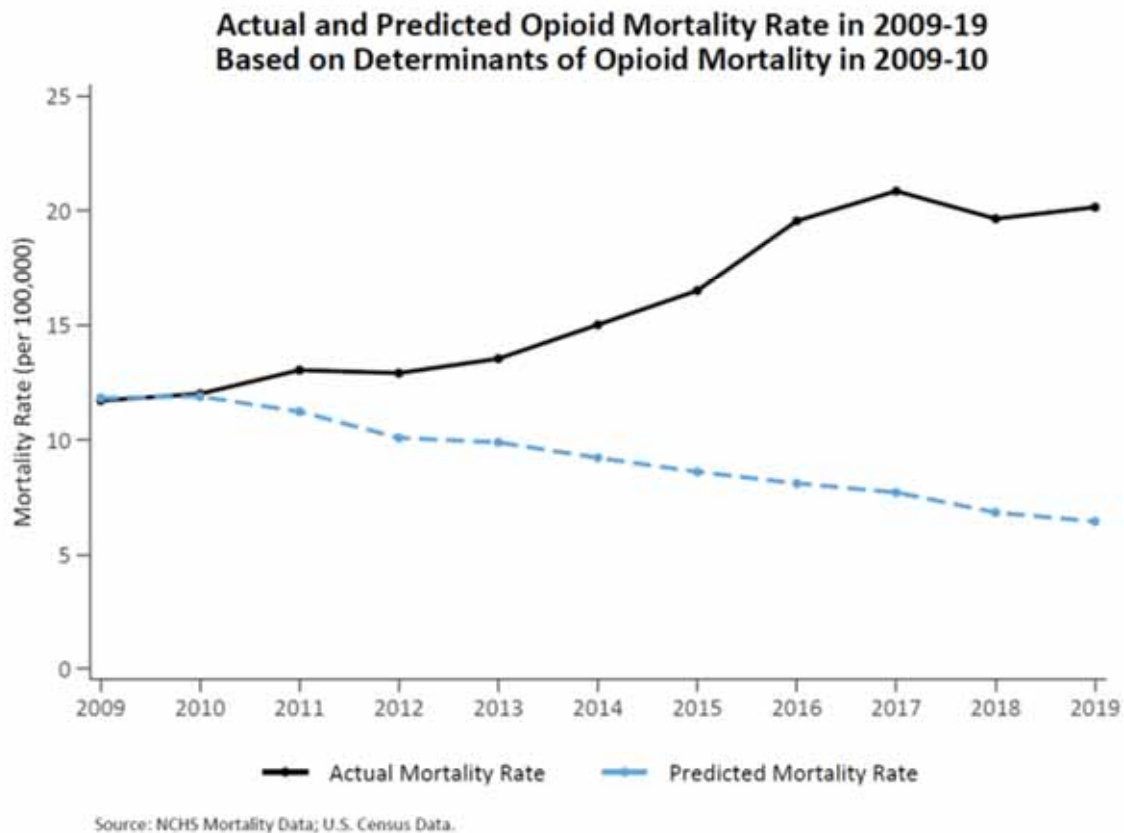
the percent under age 30, the percent white, the percent with less than a high school education, median household income, prime age male employment rate, and total population. The results of the regression, together with data on state-level changes in the demographic and economic factors used in the regression analysis, are used to project changes in the opioid mortality rate expected in the absence of the illicit opioid crisis.

125. As summarized in Exhibit 30, this indirect regression analysis implies that changes in these economic and demographic factors would have led to a decline in opioid mortality between 2010 and 2019 in the absence of the emergence of the illicit crisis. The output from this regression is summarized in Appendix 7.¹⁰⁸ This analysis provides additional evidence that the increase in opioid mortality following the structural change in 2010 cannot be attributed to economic and demographic factors and instead is the consequence of the illicit crisis that was caused by earlier shipments of prescription opioids.

¹⁰⁸ Appendix 7 also includes the results from a parallel regression based on the sample of 405 large counties.

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Exhibit 30



126. In sum, the analyses described in this section establish a large and statistically significant structural change in both prescription and illicit opioid mortality trends that closely coincide with reforms to the prescription opioid marketplace that took place in and around 2010. These reforms resulted from the prescription opioid crisis that developed during the late 1990s and 2000s. The analysis thus helps establish the causal relationship between shipments of prescription opioids prior to 2010 and the subsequent illicit opioid crisis.

127. While these analyses establish that mortality was higher in states that received higher shipments, this does not imply that areas that received lower levels of shipments were unharmed. As shown in Exhibit 6 above, shipments of prescription opioids increased in all areas from the mid-1990s through 2010. The analysis thus establishes any area that experienced an increase in shipments would realize an increase in opioid-related mortality. While the

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magnitude of the harms in areas with lower shipments is lower than in high shipment areas, low shipment areas suffered harm nonetheless.

2. Regression Estimates of the Impact of Shipments on Opioid Mortality: 2010-2019

128. Regression analysis of the relationship between post-2010 changes in illicit opioid mortality and shipments of prescription opioids between 1997-2010 provides further evidence that the illicit crisis was caused by prior shipments of prescription opioids. Like the regression analysis for mortality through 2010 described above, the analysis is based on state-level data and controls for several economic and demographic variables.

129. The results of this regression analysis are summarized in Exhibit 31. The full regression output from these models is summarized in Appendix 8. The results indicate that states with higher shipments of prescription opioids in 1997-2010 experienced significantly greater increases in illicit opioid mortality between 2010 and 2019.¹⁰⁹ Specifically, these results indicate that if prescription opioid shipments remained at levels observed in 1997 the illicit mortality rate in the U.S. in 2019 would have been 3.76 per 100,000 instead of the actual rate of 14.48. This means that shipments of prescription opioids raised the illicit opioid mortality rate by approximately 285 percent relative to the level otherwise expected.

¹⁰⁹ The analysis compares changes in the average illicit mortality rate in 2009-10 and 2018-19.

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Exhibit 31

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Change in Opioid-Related Mortality through 2019

Model	Mortality Type	Base Period	Post Period	Coefficient on Shipments				Implied Impact of Increase in Shipments on 2017-2018 Mortality Rate		
				Beta	Std. Err.	T-Stat.	P-Value	Actual Mortality Rate	Implied But-For Mortality Rate	Percent Elevation
4	Illicit Opioids	2009-2010	2018-2019	10.69	3.71	2.88	0.01	14.48	3.76	284.6%
5	Any Opioid	1993-1995	2018-2019	13.16	4.37	3.01	0.00	19.90	6.70	197.0%

Notes:

Robust standard errors.

Control variables for all regressions: Shipments per capita per day (average 1997-2010); base period non-mortality harm rate; change in percent of population white; change in median household income; change in percent less than high school; change in prime male employment to population; percentage change in total population.

Excludes DC and Puerto Rico.

130. Exhibit 31 also reports the results of a regression analysis relating per capita shipments between 1997-10 to the increase in total opioid mortality between 1993 and 2019 – the full period for which mortality data are available based on state data. The analysis yields an estimate of the average relationship between shipments and all types of opioid mortality without distinguishing between the two distinct eras of the crisis. Nonetheless, the results of the analysis again establish a large positive and statistically significant relationship between opioid mortality and shipments. These regression results imply that if shipments had remained at 1997 levels then the overall opioid mortality rate in the U.S. in 2019 would have been reduced by 13.20 per 100,000, from 19.90 to 6.70. This means that shipments of prescription opioids elevated the national opioid mortality rate by approximately 197 percent.

131. As discussed above, this regression is likely to understate the true impact of shipments on opioid-related mortality due to the limitations in available data, including the absence of information on average prescription duration and average dosage size. Moreover,

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for the reasons discussed above, the increase in illicit opioid mortality was caused by shipments of prescription opioids, but this analysis does not attribute the full increase to prior shipments. Instead this calculation reflects only the portion of the increase that is captured by regression estimates of the relationship between shipments and opioid mortality across states. For the reasons discussed above, it is reasonable to conclude that the entire increase in illicit mortality is attributable to the Phase 2 reforms that were implemented due to prior shipments, and that in the absence of this history, illicit opioid mortality would have continued to be stable after 2010, just as it had been for the prior 15 years.

132. As noted above, I have performed a parallel set of regression analyses describing the relationships between changes in opioid mortality and per capita shipments for large counties instead of states. These results are reported in Appendix 9 and the results are consistent with the conclusions expressed above. The county-specific data includes information on 405 large counties, expanding the size of the sample and the precision of the regression estimates and permitting inclusion of additional economic and demographic variables. Like results based on state data, the county-level analysis identifies a sizeable and statistically significant relationship between shipments of prescription opioids between 1997-2010 and: (i) the growth of prescription opioid mortality through 2010; (ii) the growth of illicit opioid mortality between 2010 and 2018; and (iii) the overall growth in opioid mortality between 1993 and 2018. Appendix 9 also summarizes differences in the results based on county-level and state-level data.

133. In sum, the regression analysis, together with the structural change analysis (and additional analysis investigating alternative explanations of the opioid crisis presented in Section VI below), establish that shipments of prescription opioids in the 1990s and 2000s

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caused the elevation in both prescription and illicit opioid mortality. This conclusion is further supported by a growing literature in economics, which has applied a variety of econometric techniques to evaluate the relationship between shipments of prescription opioids and growth in opioid-related mortality. Similar conclusions have also been reached in a variety of epidemiological studies. A brief review of this literature, including peer reviewed studies and working papers from economists and epidemiologists, is presented in Appendix 10. Based on the analyses presented in this section along with this growing literature, I conclude that defendants' shipments caused the increase in opioid-related harms.

V. Other Opioid-Related Harms Were Caused by Shipments of Prescription Opioids

134. This section summarizes my analysis of the impact of shipments of prescription opioids on a variety of metrics of opioid-related harms including rates of HUD and OUD, NAS, opioid-related emergency department visits and hospital admissions and foster care placements. My analysis of these metrics uses state-level data.¹¹⁰ The opioid crisis is also associated with other social harms not directly addressed here, including increases in crime, homelessness, and risks of contracting HIV and hepatitis C, among others.¹¹¹ The metrics

¹¹⁰ County-level data on these metrics are not generally available.

¹¹¹ In the CT1 phase of this litigation, I submitted an expert report that included regression analysis of the relationship between shipments of opioids and crime using county-level data. I concluded that there was a positive and statistically significant relationship between opioid shipments and crime. (Expert Report of David Cutler, March 25, 2019, Section VIII) Examples of studies relating opioid use to other social harms include: Winkelman, Tyler N.A. V.W. Chang, and I.A. Binswanger, "Health, Polysubstance Use, and Criminal Justice Involvement Among Adults with Varying Levels of Opioid Use," *JAMA Open Network*, 1(3), 2018, pp. 1-12; National Alliance to End Homelessness, "Opioid Abuse and Homelessness," April 5, 2016, available at <https://endhomelessness.org/resource/opioid-abuse-and-homelessness/>; Iheanacho, Thaddeus, Elina Stefanovics and Robert Rosenheck. "Opioid use disorder and homelessness in the Veterans Health Administration: The challenge of multimorbidity." *Journal of Opioid Management* 14, no. 3 (May/June 2018): 171-182; CDC, "Support to Address the Infectious Disease Consequences of the Opioid Crisis," available at <https://www.cdc.gov/pwido.html>; CDC Press Release, "Increase in hepatitis C infections linked to worsening opioid crisis," December 21, 2017, available at <https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html>.

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analyzed here are representative examples that establish the impact of shipments on a range of social harms.

135. As in my analysis of the relationship between shipments and mortality, there are two prongs to my analysis of non-mortality harms. First, as above, I compare trends in harms in states that account for the 25 percent of the population with the highest level of shipments (“high shipment states”) and states that account for 25 percent of the population with the lowest level of shipments (“low shipment states”).¹¹² Next, I report the results of a series of regression analyses that relate changes in metrics of opioid-related harms in a state to shipments. These analyses control for a variety of state-specific economic and demographic characteristics.

136. My analysis focuses on comparisons of both changes over time in these metrics across high and low shipment states as well as differences in the most recent available data. This is because available data typically do not cover the “pre-epidemic period” so initial levels of harms may in fact reflect the impact of prior shipments of prescription opioids as well as other factors. To the extent that shipments of prescription opioids are associated with adverse outcomes, I expect that the metrics of opioid-related harms would generally be higher and grow more over time in high-shipment states relative to low-shipment states.¹¹³ Section A below compares opioid-related harms in high and low shipment states and Section B presents regression analyses of these relationships.

¹¹² These comparisons use available data on all high and low shipment states. The results are not materially altered if the analysis is limited to states that report data in all years.

¹¹³ As noted earlier, per capita shipments were more than 95 percent higher in the high shipment states compared to the low shipment states over the 1997 through 2010 period.

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A. Comparison of Levels and Trends in Opioid-Related Harms in High and Low Shipment States

137. Consistent with the conclusion that opioid-related harms are caused by shipments of prescription opioids, I find that harms have grown more rapidly in high shipment states compared to low shipment states.

1. OUD / HUD

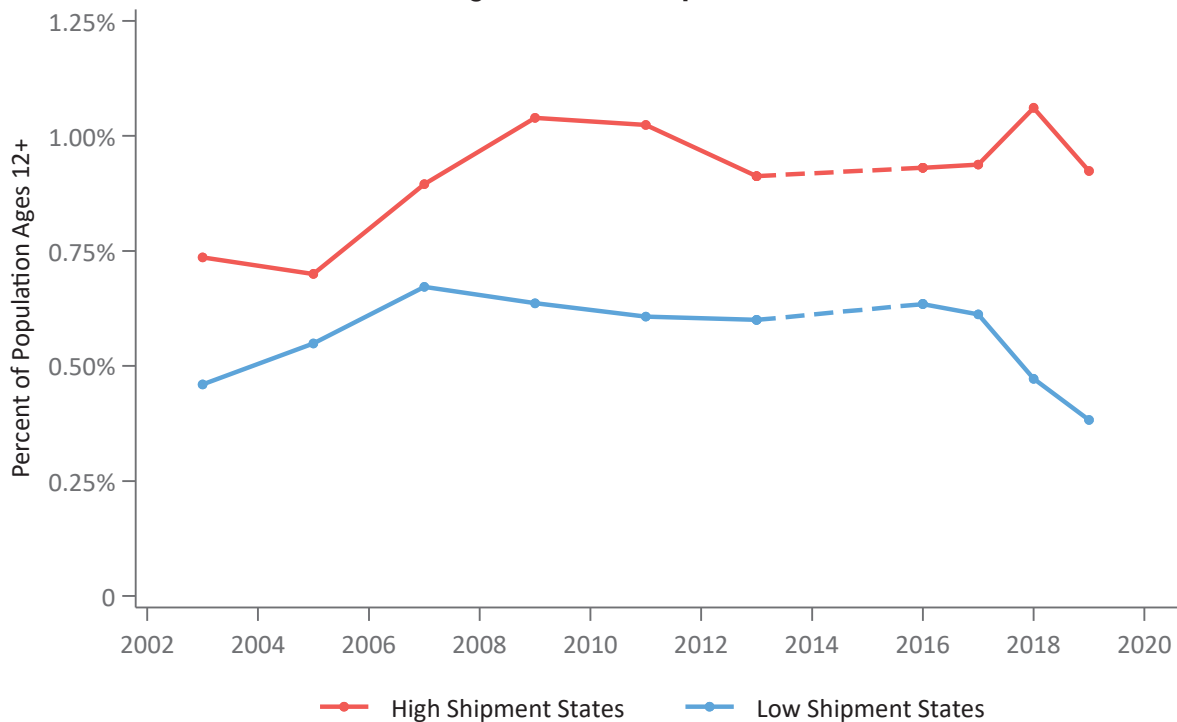
138. As discussed in Section III.D above, estimates of OUD and HUD are available from the NSDUH survey for 2002-03 through 2018-19 and NSDUH reports state-specific data as two-year averages.¹¹⁴ Also discussed above, it is widely recognized that the NSDUH survey undercounts opioid misuse and use disorder and that the definition of OUD has been revised over time although the definition of HUD has not.

- Exhibit 32 reports NSDUH-based measures of OUD expressed as a percent of the population ages 12 and above in high and low shipment states from 2002-03 through 2018-19. OUD includes disorders associated with both pain relievers and heroin. High shipment states have had higher levels of OUD in all years since 2002-03, and the gap between high and low shipment states grew over time: in 2002-03, OUD in high shipment states was 60 percent higher than in low shipment states and in 2018-19 the gap was 141 percent.

¹¹⁴ Prior to 2015, data are reported biennially (e.g., 2003-04, and 2005-06). After 2015, data are reported as two-year averages on an annual basis (e.g., 2015-16, 2016-17).

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Exhibit 32

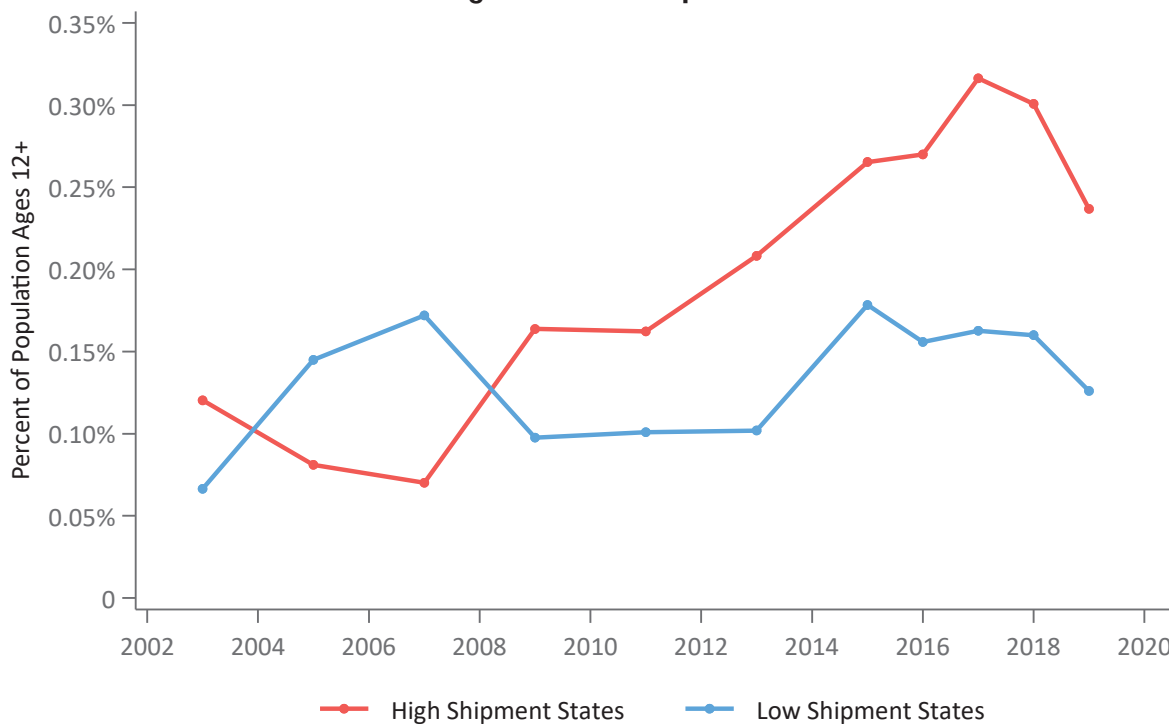
NSDUH Opioid Use Disorder Rate
High vs. Low Shipment States

Note: NSDUH revised questions regarding pain reliever use/abuse in 2015.
 Questions regarding heroin use/abuse are unaffected by this change.
 Source: NSDUH.

- Exhibit 33 reports changes over time in NSDUH based estimates of HUD between 2002-03 and 2018-19. As the figure indicates, in 2018-19, HUD in high shipment states was 88 percent higher than in low shipment states. Prior to 2010-11, reported HUD rates in high and low shipment states varied substantially from year to year with little difference in average rates between 2003-04 and 2010-11, prior to the illicit opioid epidemic. However, HUD in high shipment states grew relative to low shipment states after 2010-11. These patterns are consistent with the view that the increases in HUD after 2011 are the consequence of prior shipments of prescription opioids.

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Exhibit 33

NSDUH Heroin Use Disorder Rate
High vs. Low Shipment States

Note: NSDUH revised questions regarding pain reliever use/abuse in 2015.
 Questions regarding heroin use/abuse are unaffected by this change.
 Source: NSDUH.

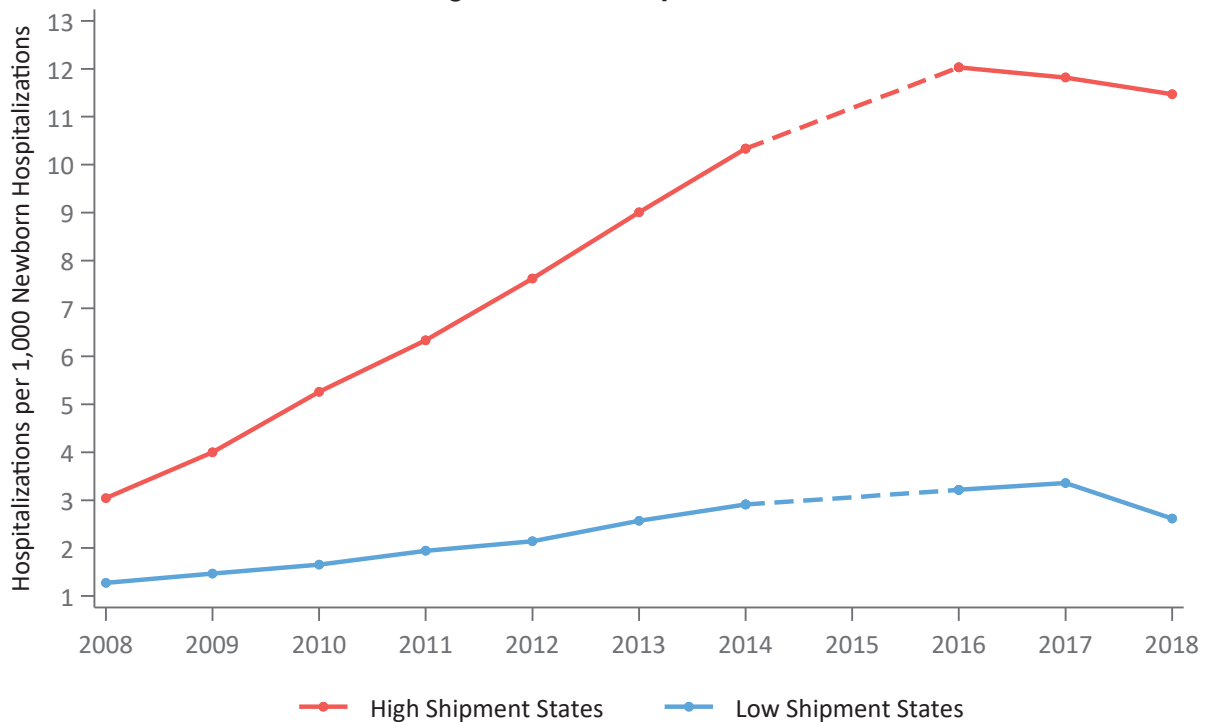
2. Neonatal Abstinence Syndrome

139. As described above, data on NAS rates by state are provided by HCUP for the period of 2008-18. NAS rates in high shipment states are more than three times as high as low shipment states in 2018, the most recent data available. As shown in Exhibit 34, NAS rates in high shipment states were already more than twice as high as in low shipment states in 2008. Since that time the gap between high and low shipment states has increased steadily. Between 2008 and 2018, NAS rates grew 277 percent in high shipment states from already elevated levels compared to 105 percent in low shipment states.

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Exhibit 34

NAS Hospitalization Rate High vs. Low Shipment States



Note: 2008-2014 data are based on ICD-9 while 2016-2018 are based on ICD-10.
Full statistics are not available for 2015 because the ICD-9 to ICD-10 transition occurred on 10/01/2015.
Source: HCUP.

3. Opioid-Related Emergency Department Visits and Hospital Admissions

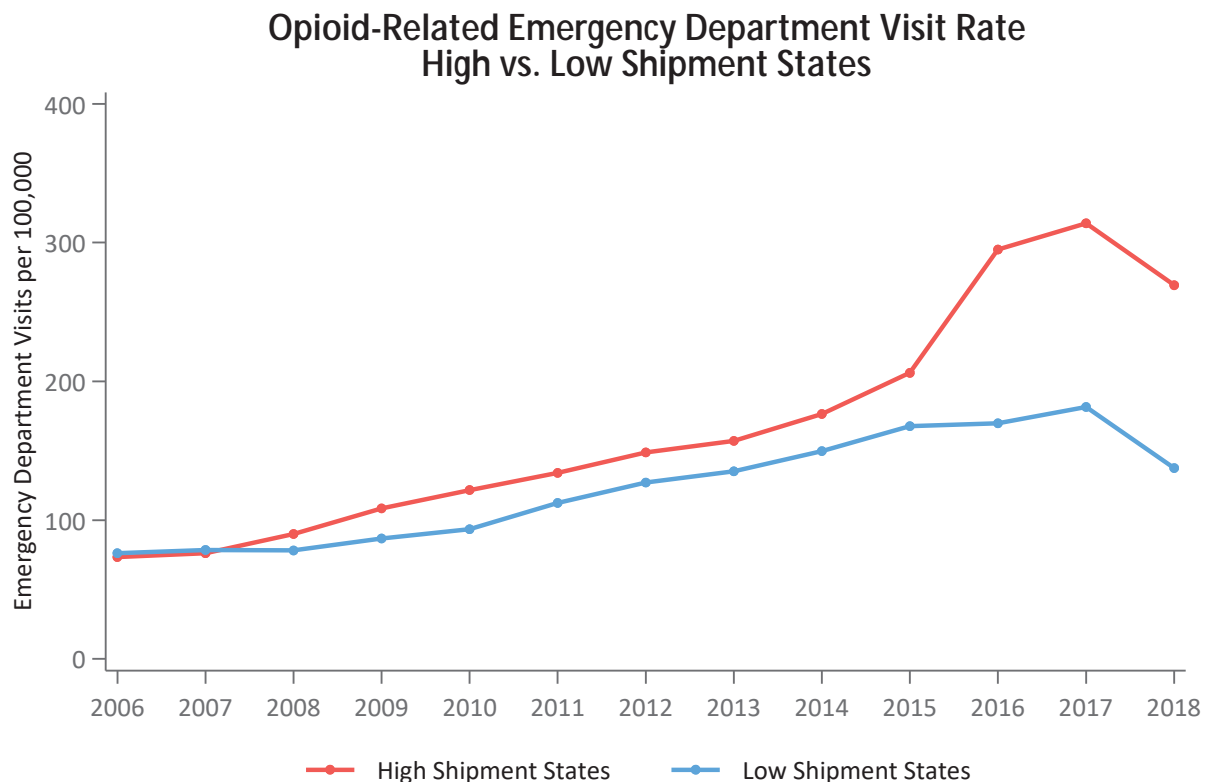
140. As described in Section III.D, HCUP reports opioid-related emergency department visits and hospital admissions on a per capita basis by state. Interpretation of these data is complicated by a variety of factors including (i) growth in the number of states that participate in the program; (ii) differences in the states reporting inpatient admissions and emergency department visits; and (iii) changes in the International Classification of Diseases in 2015 that affected the definition of opioid-related events.¹¹⁵

¹¹⁵ The data do not distinguish between events associated with prescription and illicit opioids.

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141. As shown in Exhibit 35, rates of opioid-related emergency department visits were similar in high and low shipment states in 2006. By 2015, opioid-related emergency department visits per capita were 23 percent higher in high shipment states than low shipment states and by 2018, near the peak (thus far) of the illicit opioid crisis, the gap was 96 percent.

Exhibit 35



Note: Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
Source: HCUP.

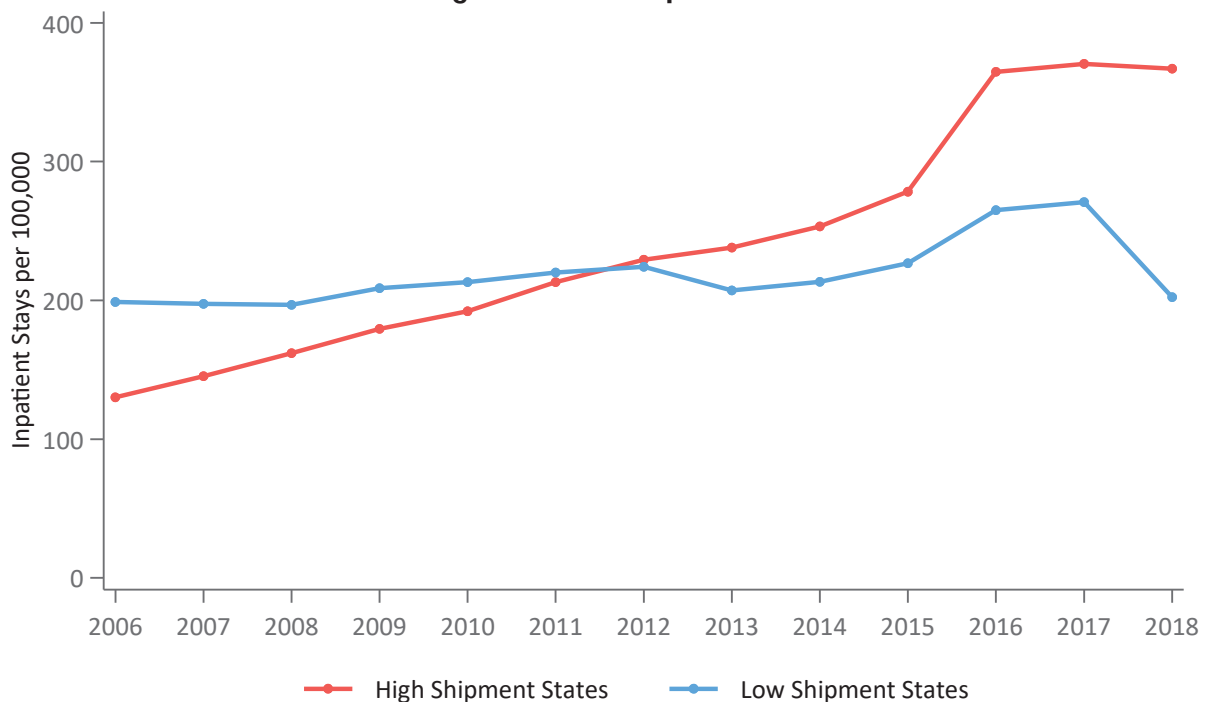
142. In 2018, the most recent year for which data are available, the rate of opioid-related inpatient stays was 81 percent higher in high shipment states than in low shipment states. As shown in Exhibit 36, opioid-related inpatient hospital stays also grew more in high shipment states than in low shipment states. Between 2006 and 2018, the rate of opioid-

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related inpatient stays grew 182 percent in high shipment states while growing by only 2 percent in low shipment states.

Exhibit 36

Opioid-Related Inpatient Stay Rate High vs. Low Shipment States



Note: Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
Source: HCUP.

4. Foster Care

143. As discussed in Section III.D above, the opioid epidemic has resulted in increased caseloads for the child welfare system. The increase in foster care placements starting in 2012 reversed a trend dating to the early 2000s of declining rates of foster care placements of more than 30 percent.¹¹⁶

¹¹⁶ See Table 11.3, National Estimates of Foster Care Use, FY1982-FY2015, Green Book of House Ways and Means Committee (2018), <https://greenbook-waysandmeans.house.gov/sites/greenbook.waysandmeans.house.gov/files/Figure%2011-3%20and%20Table%2011-3.pdf>.

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144. State-level data on foster care placements are available for 2005-19 from the HHS's Adoption and Foster Care Analysis and Reporting System (AFCARS). As previously noted, foster care placements vary widely across states for reasons unrelated to opioids and vary within states over time. The national placement rate fell 21 percent between 2005 and 2010.

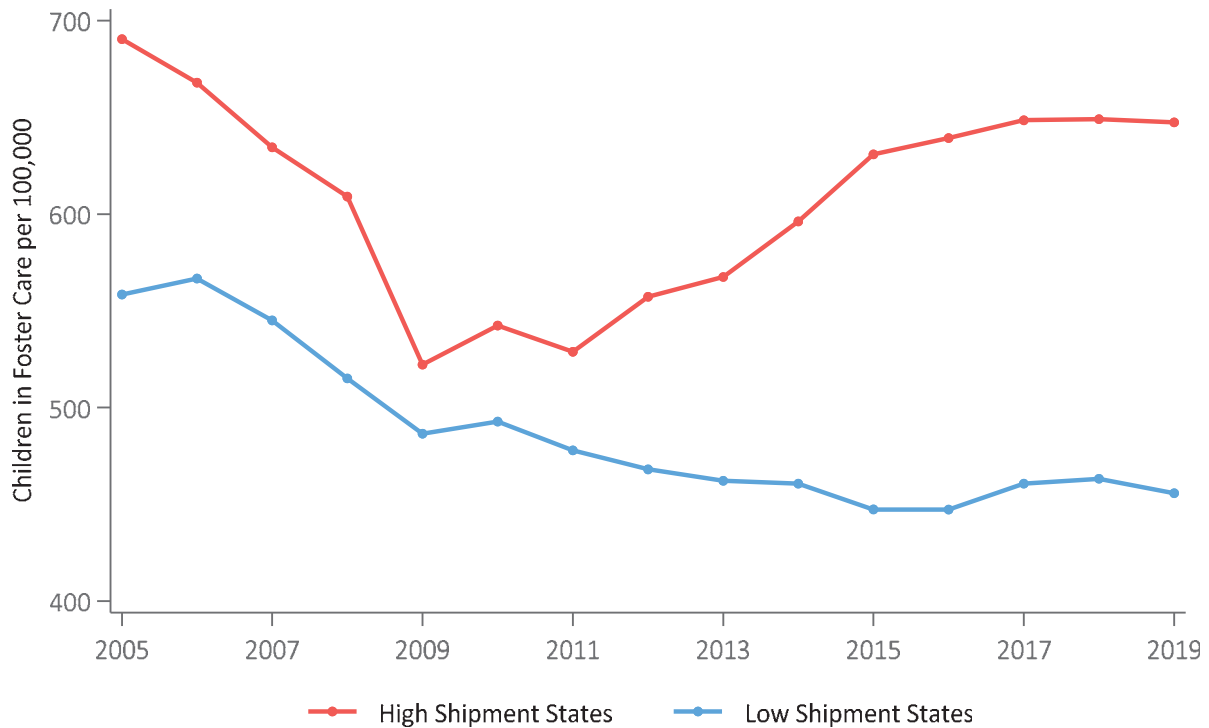
145. Exhibit 37 compares trends in foster care placements (per 100,000 children ages 0-19) in high and low shipment states. In 2019, the most recent year of data available, foster care placements were 42 percent higher in high shipment states than in low shipment states. In 2005, foster care placement rates in high shipment states exceeded those in low shipment states. In both high and low shipment states, foster care placement rates decreased through 2011, the continuation of the longer-term declines in foster care placements mentioned above.¹¹⁷ After 2011, however, foster care placement rates in low shipment states continued to decrease, although at a slower pace, while rates in high shipment states increased 22 percent. Thus, following the start of the illicit opioid crisis, the gap between high and low shipment states increased from 51 per 100,000 children in 2011 to 192 in 2019. Again, these results are consistent with the view that shipments of prescription opioids in earlier years resulted in higher foster care placements.

¹¹⁷ See Table 11.3 of Green Book of House Ways and Means Committee, <https://greenbook-waysandmeans.house.gov/sites/greenbook.waysandmeans.house.gov/files/Figure%2011-3%20and%20Table%2011-3.pdf> (undated).

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Exhibit 37

Rate of Children in Foster Care High vs. Low Shipment States



Source: AFCARS.

B. Regression Analysis of the Relationship Between Shipments and Other Opioid-Related Harms.

146. I have also used regression analysis to evaluate the relationship between opioid-related harms other than mortality and shipments of prescription opioids to a state between 1997 and 2010. As discussed above, the data on non-mortality harms are less complete than the data on mortality and are typically not available for all years that encompass the opioid crisis or for the pre-crisis period. In some cases, the data are available for only a limited number of states.

147. The regression analysis presented in this section controls for other factors affecting changes in harms over time for each state including: the percent change in state

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population; the change in median household income; the change in the share of prime age males that are employed; the change in the percentage of the population that is white; and the change in the share of the population with less than high school degree. The analysis also controls for the initial level of the relevant harm, which captures potential “regression to the mean,” – the idea that states with a particularly high or low level of harm in a given year are likely to revert to the state average in subsequent years.

148. The results are reported in Exhibit 38. The complete output from these regressions is presented in Appendix 11. The regression analyses establish a positive relationship between shipments of prescription opioids to a state between 1997 and 2010 and changes over the time period covered by the available data for each of the opioid-related harms: OUD, HUD, NAS, opioid-related visits to emergency department, opioid-related hospital admissions, and foster care placements. The estimated relationship between shipments and emergency department visits, while positive, is not statistically significant.¹¹⁸ This is not surprising due to the limited size of the sample (24 states). The estimated relationship between shipments and foster care placements is marginally significant (p-value of .109), and all other estimates are highly significant (with p-values below .02). These results further establish the causal relationship between shipments of prescription opioids and harms.

¹¹⁸ The p-value reflects the probability that a result at least as large as the one observed will be observed assuming the maintained hypothesis (here, that harms are unrelated to shipments) is true. P-values less than .05 are often described as “statistically significant” but that is not a bright line rule.

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Exhibit 38

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Changes in Non-Mortality Harms

Model	Harm Category	Base Period	Post Period	Number of States	Coefficient on Shipments			
					Beta	Std. Err.	T-Stat.	P-Value
1	Opioid Use Disorder Rate	2002-2003	2018-2019	50	416.34	117.58	3.54	0.00
2	Heroin Use Disorder Rate	2002-2003	2018-2019	50	163.57	60.96	2.68	0.01
3	NAS Hospitalization Rate	2008-2009	2017-2018	42	7.52	3.02	2.49	0.02
4	Emergency Department Visit Rate	2006-2007	2017-2018	24	74.49	78.79	0.95	0.36
5	Inpatient Stay Rate	2006-2007	2017-2018	38	134.01	30.49	4.40	0.00
6	Rate of Children in Foster Care	2010-2011	2018-2019	50	161.17	98.41	1.64	0.11

Notes:

Control variables for all regressions: Shipments per capita per day (average 1997-2010); base period non-mortality harm rate; change in percent of population white; change in median household income; change in percent less than high school; change in prime male employment to population; percentage change in total population.

Robust standard errors.

NAS is measured as rate per 1,000 hospital births; other metrics measured as rate per 100,000 state residents.

VI. Demand Side Factors Play Only a Modest Role in Explaining the Opioid Crisis

149. As discussed above, some researchers have stressed the role of “demand side” factors as potential drivers of opioid abuse and mortality. Anne Case and Angus Deaton, for example, stress the role of depression, despair, social isolation, and increased prevalence of pain as factors driving a range of “Deaths of Despair,” including increased opioid mortality.¹¹⁹

150. This section establishes that the supply of prescription opioids, not demand side factors, is the principal driver of increases in mortality and other opioid-related harms. I first review several metrics that establish that in recent years opioid-related mortality rose more rapidly than other types of mortality associated with depression, despair, social isolation and pain. I also show that “high shipment” states have materially higher rates of opioid mortality but not of other types of “Deaths of Despair.” This is a form of “placebo analysis” that further

¹¹⁹ Case and Deaton (2017), p. 398. Case and Deaton argue that supply of opioids was not the “fundamental factor” responsible for the phenomenon they identify, but they argue that it “added fuel to the flames, making the epidemic much worse than it otherwise would have been.” (at p. 399). See also, Case, Anne and Angus Deaton, *Deaths of Despair and the Future of Capitalism*, Princeton: Princeton University Press (2020).

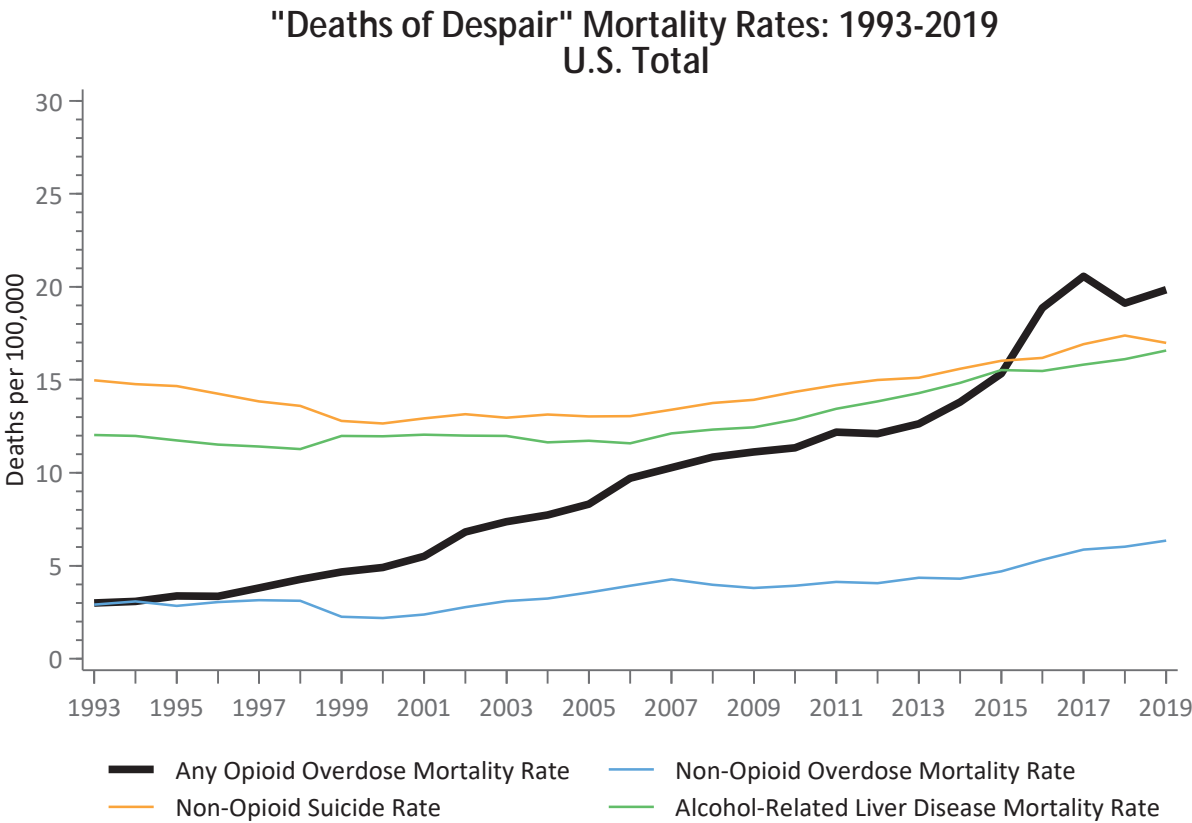
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establishes that the high levels of opioid mortality in high shipment states is not due to unobserved factors that drive a broader set of deaths related to social conditions.

A. Opioid Mortality Has Grown More Rapidly than Other “Deaths of Despair”

151. Deaths of despair, as defined by Case and Deaton, includes drug-related overdose deaths, suicides, and alcohol-related liver disease. Exhibit 39 summarizes trends in opioid-related mortality as well as the three categories of deaths of despair from 1993-2019 based on MCODE data.¹²⁰

Exhibit 39



Source: NCHS Mortality Data and Census Data.

¹²⁰ Data on non-opioid drug overdoses are based on those with identified causes (e.g., cocaine or methamphetamines) and exclude unclassified drug overdoses.

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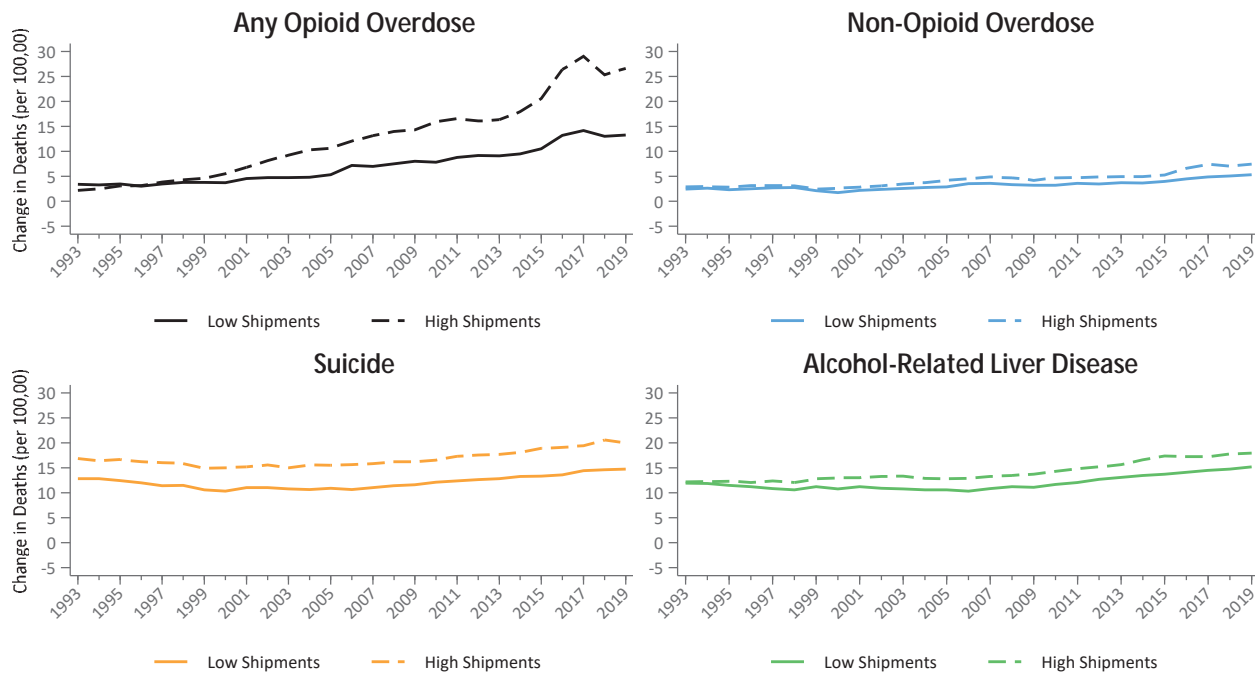
152. Exhibit 40 demonstrates that the growth of non-opioid deaths of despair is not related to dispensing and shipments of prescription opioids. As shown in the top left quadrant, opioid mortality grew more rapidly in high-shipment states relative to low-shipment states. However, there is no material difference in trends in high and low shipment states for the other types of deaths of despair.¹²¹ These results establish that the observed relationship between shipments and opioid mortality is not due to unobserved factors correlated with shipments that affect the broader categories of deaths of despair. Because there is no necessary basis for shipments to materially affect non-opioid mortality, this analysis provides a type of “placebo” test that verifies that the relationship between shipments and opioid mortality is, in fact, causal. The exhibit compares the increase in each death of despair category in high and low shipment states since 1993.

¹²¹ Statistical analysis indicates that the difference between high and low shipment states in opioid mortality trends is larger than the corresponding difference for the other death of despair categories, and that these differences are statistically significant.

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Exhibit 40

Mortality Rate by "Deaths of Despair" Category and State Shipment Level Change in Mortality Rate Relative to 1993-95 Average



Source: NCHS Mortality Data and Census Data.

B. Economic Studies Show That Demand Factors Fail to Explain the Dramatic Increases in Opioid Mortality

153. Economists evaluating the opioid epidemic have shown that while demand factors are related to the growth in opioid overdose deaths, demand factors quantitatively fail to explain the vast bulk of the increase in deaths. This leads to the conclusion that supply factors (such as supply of prescription opioids) play a key role. For example, Ruhm (2019) analyzes county-level data on drug overdose deaths and finds that economic factors such as the poverty rate, unemployment rate, home prices, and the exposure of local employment to imports explain very little of the increase in mortality between 1999 and 2015.¹²² Ruhm

¹²² Ruhm, Christopher J., "Drivers of the Fatal Drug Epidemic," *Journal of Health Economics* vol. 64 (2019), pp. 25-42, at p. 26.

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concludes that: “While these results do not completely eliminate a possible contribution of demand-side mechanisms, they strongly suggest the efficacy of policies aimed at addressing the availability, cost and risky use of drugs.”¹²³

154. Dow, Godoy, Lowenstein, and Reich (2019) analyze whether economic policies including minimum wage increases and expansion of the earned income tax credit have causal effects on deaths of despair, including drug overdoses. They find that while higher minimum wages and earned income tax credits lead to lower rates of non-drug related deaths of despair, there is no significant effect of these policies on drug overdose deaths (either intentional or unintentional).¹²⁴ This is consistent with my analysis above, which shows that opioid-related overdoses have increased substantially more than other categories of deaths of despair and are due to shipments, not demand-side factors.

155. Currie and Schwandt (2020) analyze whether labor market conditions explain the increase in opioid related mortality. They conclude: “There is little relationship between the opioid crisis and contemporaneous measures of labor market opportunity. Cohorts and areas that experienced poor labor market conditions do show lagged increases in opioid mortality, but the effect is modest relative to the scale of the epidemic.”¹²⁵

¹²³ Id.

¹²⁴ Dow, William H., Anna Godøy, Christopher A. Lowenstein and Michael Reich, “Can Economic Policies Reduce Deaths of Despair?,” Institute for Research on Labor and Employment Working Paper #104-19, April 2019.

¹²⁵ Currie, Janet and Hannes Schwandt, “The Opioid Epidemic Was Not Caused by Economic Distress But by Factors that Could Be More Rapidly Addressed,” NBER Working Paper No. 27544, July 2020, Revised August 2020.

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CONCLUSIONS TO CHAPTER 1

156. Abuse of prescription and illicit opioids has generated a public health crisis that has resulted in increased mortality, opioid use disorder (OUD), heroin use disorder (HUD), neonatal abstinence syndrome (NAS), foster care placements, and opioid-related inpatient hospital admissions and emergency department visits. My analysis establishes a causal relationship between the dramatic growth in shipments of prescription opioid from the late 1990s through 2010 and (i) large increases since that time in overdoses from prescription opioids; and (ii) large increases in overdoses from illicit opioids after 2010; and (iii) increases in a variety of other opioid-related harms. To the extent that manufacturers, distributors, or dispensers failed to meet their obligations to maintain effective controls against diversion of opioids and to identify suspicious patterns that should have been investigated and cleared before dispensing, their misconduct had a causal relationship to mortality from prescription and illicit opioids and other opioid-related harms.

157. In sum, my analysis establishes that it was the widespread availability of prescription opioids, not other economic and social trends, that caused the large nationwide increases in opioid-related mortality and significant increases in other opioid-related harms, including OUD, HUD, NAS, opioid-related hospital admissions, and foster care placements.

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Chapter 2: The Opioid Crisis in Lake and Trumbull Counties

VII. Introduction

158. I have been asked by Counsel for Lake and Trumbull counties to evaluate the following questions:

- How do opioid-related shipments to Lake and Trumbull counties compare to national patterns?
- How do patterns of prescription opioid mortality, illicit opioid mortality, and other opioid-related harms in Lake and Trumbull counties, and Ohio in total, compare to national patterns?
- How has the opioid crisis affected OUD, HUD, NAS, foster care placements, and opioid-related inpatient hospital admissions and emergency department visits in the area?
- How much of the harms from opioids in Lake and Trumbull counties can be attributed to defendants in this matter?

159. My major conclusions are as follows:

- Shipments to Trumbull and Lake counties grew dramatically between 1997 and 2010, with shipments to Trumbull County above the national average and shipments to Lake County below that average.
- Shipments to Trumbull and Lake counties declined substantially between 2010 and 2019, with percentage declines comparable to the national average.

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- Opioid mortality grew substantially in Trumbull and Lake counties between 1999 and 2010, with mortality in Trumbull County exceeding the national average and mortality in Lake County below the national average.
- In both Trumbull and Lake counties, most of the increase in opioid mortality through 2010 is attributable to prescription opioids, although illicit opioid mortality in both areas grew between 2005-10.
- Opioid mortality in Trumbull and Lake counties grew rapidly after 2010. In both areas, increases substantially exceeded the national average, with the growth in Trumbull County among the highest of large counties in the U.S. Prescription opioid mortality fell in both counties after 2010, but that decrease was more than offset by dramatic increases in illicit opioid mortality.
- The dramatic increases in illicit opioid mortality were facilitated by the shipments of prescription opioids and the availability of powdered heroin in the area prior to 2010. The increase in illicit mortality in the area prior to 2010 reflected the same forces that generated the more widespread illicit opioid crisis after 2010.
- Opioid-related harms other than mortality grew more rapidly in Ohio than nationally over the past 15 years. The growth of NAS and opioid-related emergency department visits and hospital admissions substantially exceed the national average.
- In Ohio, like the U.S. as a whole, opioid-related mortality grew far more rapidly than other types of “deaths of despair,” indicating that supply factors – not demand factors – are the principal drivers of opioid-related mortality.

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- Together with analysis by other experts, my analysis establishes that defendants' misconduct resulted in substantial harms to Lake and Trumbull Counties.

160. The remainder of this chapter documents the evolution of the opioid crisis in Trumbull and Lake counties and Ohio as a whole. Section VIII reviews information on the economic impact of the crisis in these counties and nearby areas and documents the history of shipments of prescription opioids, the growth of prescription opioid mortality since the mid-1990s, and the increase in illicit opioid mortality since 2010.¹²⁶ Section IX builds upon the regression analyses summarized in Chapter 1 in order to determine the share of opioid-related mortality that is attributable to defendant dispensers' misconduct. Finally, Section X documents the emergence of non-mortality opioid-related harms in Trumbull and Lake counties and Ohio.

VIII. Shipments and Opioid-Related Mortality in Trumbull and Lake Counties.

A. Background

161. Trumbull and Lake counties, and Ohio more generally, have been particularly hard hit by the opioid epidemic. The CDC's MCOD data indicate that between 1999 and 2019, more than 930 Trumbull County residents and nearly 700 Lake County residents died of opioid overdoses. Over this period, the opioid mortality rate in Trumbull County was 117 percent above the national average and the rate in Lake County was 50 percent above the national average. These differences are largely attributable to high illicit mortality in these areas since 2010. In 2018-19, illicit mortality in Trumbull County was roughly triple the national average while the rate in Lake County was roughly double the national average.

¹²⁶ State level data are used because county-level data on non-mortality harms are not generally available on a county level.

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162. The economic impact of the crisis on the area has been significant. As discussed in Section II.A above, various studies estimate the economic impact of the opioid crisis on the U.S. Related studies have focused on the costs in Lake and Trumbull counties as well as nearby areas:

- Rembert, et. al (2017) of the Ohio State University scale national estimates of opioid related costs from Florence, et al. (2016)¹²⁷ and the CDC to estimate the costs specific to Ohio in 2015.¹²⁸ They estimate fatal and non-fatal (health care, treatment, criminal justice, lost productivity) opioid-related costs of \$6.6 billion to \$8.8 billion for Ohio in 2015, translating to an average of \$560 to \$756 per Ohio resident. They estimate that per capita costs in Trumbull County were among the highest of county-specific cost estimates (more than \$1,000 per capita in 2015) and per capita costs in Lake County were between \$500 and \$1,000 per capita.
- Altarum, a health research and consulting firm, estimated that the opioid epidemic imposed economic costs of \$200 million in 2016 in Lorain County, Ohio, which is near Lake and Trumbull counties.¹²⁹ This includes estimates of costs related to lost earnings and productivity, healthcare, criminal justice, child and family assistance and treatment and prevention efforts.

163. The opioid epidemic has also strained government resources in Lake and Trumbull counties. For example:

¹²⁷ See discussion of this study in Section II.A above.

¹²⁸ Rembert, Mark, Michael Betz, Bo Feng and Mark Partridge, "Taking Measure of Ohio's Opioid Crisis," October 2017, pp. 8-9.

¹²⁹ Altarum, "Community Assessment of the Opioid Crisis in Lorain County, Ohio: Executive Summary," December 20, 2017, p. 2.

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- Lake County began operating an opioid task force in 2010 and expanded addiction treatment services for children, adolescents, adults, seniors, and special populations, including in jails, treatment centers, and schools.¹³⁰ The task force includes representatives from various departments and divisions in Lake County, including courts, law enforcement, first responders, education, and the offices of the Lake County Coroner, the General Health District, and the Department of Job and Family Services.¹³¹
- In a 2018 summary, Lake County's Alcohol, Drug Addiction and Mental Health Services (ADAMHS) Board detailed the prevention, treatment, and other related services and programs offered to treat opioid abuse and addiction, including early childhood intervention, school-based and home-based programs, prescriber education, and community outreach.¹³² Lake County's ADAMHS Board also identified 12 different treatment and harm reduction programs being implemented, including medication-assisted treatment (MAT), treatment for OUD during pregnancy, treatment for NAS, recovery housing, peer support, and distribution of naloxone.¹³³
- Similarly, the Trumbull County Mental Health and Recovery Board served approximately 1,600 individuals with a primary diagnosis of OUD in each year during the 2017-18 period. While these clients represented only approximately 14

¹³⁰ Lake County ADAMHS Board, "The Opiate Epidemic: How we're fighting back," June 28, 2017, ADAMHS000005041, at pp. 19, 31.

¹³¹ Lake County ADAMHS Board, "The Opiate Epidemic," June 13, 2018, ADAMHS000005383, at p. 35.

¹³² Lake County ADAMHS Board, "County Hub Program to Combat Opioid Addiction – Initial Report," October 2018, LAKE002430160 at 160-176.

¹³³ Lake County ADAMHS Board, "County Hub Program to Combat Opioid Addiction – Initial Report," October 2018, LAKE002430160 at 165-166.

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percent of clients among the top 10 diagnoses served annually, they accounted for nearly 50 percent of these agency costs. The average annual cost per client in 2017 was nearly \$7,000 for clients with a primary diagnosis of OUD, compared to approximately \$1,000 for clients with other primary diagnoses.¹³⁴ Data from 2018 exhibited similar patterns, with an average annual cost per OUD client of nearly \$5,000, compared to less than \$1,000 for other primary diagnoses.¹³⁵

- Lake County has experienced increases in demand for their Children's Services Department. For instance, despite a 10 percent decrease in funding revenue from 2010 through 2016, Lake County's Children's Services Department reported a 38 percent increase in the number of children placed in custody as a result of the opioid crisis.¹³⁶
- Similarly, Trumbull County Children Services reported that in 2016, due to the opioid epidemic, paid placement costs increased by \$1 million (93 percent) from prior year levels, youth transferred from custody to relatives increased by 55 percent, and youth removed from their homes and placed directly with kin increased by 24 percent.¹³⁷

B. Shipments of Prescription Opioids to Lake and Trumbull Counties

164. Per capita shipments of prescription opioids to Trumbull and Lake counties were roughly consistent with national levels and trends between 1997 and 2010, the peak year of shipments to both counties. As shown in Exhibit 41 below, per capita shipments to Trumbull

¹³⁴ Trumbull County Health and Recovery Board, 2017 presentation, TRUM004687182, at p. 4.

¹³⁵ 2018 Trumbull Mortality and Morbidity Summary, TRUM000004170, at p. 3.

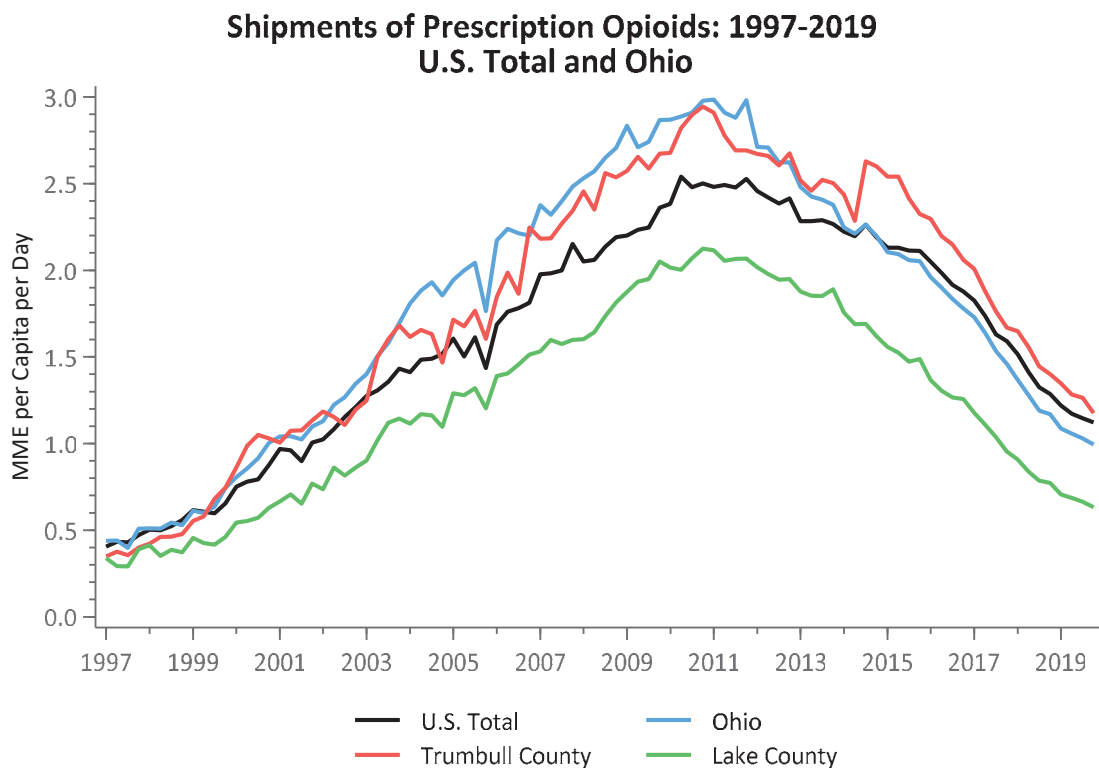
¹³⁶ Lake County Children's Services, "The need is real. The numbers tell the story," October 12, 2017, LAKE002733774.

¹³⁷ Trumbull County Children Services, 2016 Annual Report, TRUM000002982, at 985.

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County grew more rapidly than the national average over this period and closely tracked statewide trends. Shipments to Lake County were lower than the national average between 1997 and 2010, but still increased by more than 500 percent over this period. In 2010, per capita shipments to Trumbull County were 15 percent above the national average while shipments to Lake County were 17 percent below the average. Among counties in the large county sample, Trumbull ranked 133rd and Lake ranked 274th in terms of per capita shipments in 2010.¹³⁸

Exhibit 41



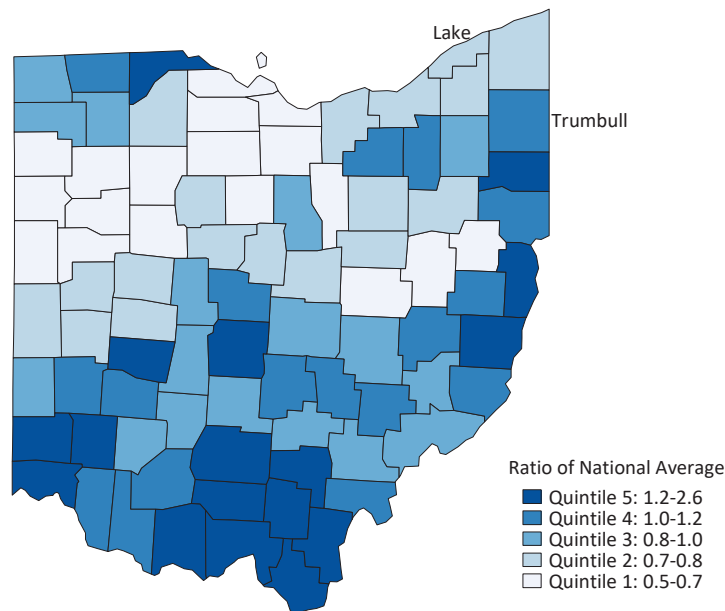
¹³⁸ As described in Appendix 3, some of my analysis is applied to 405 “large” counties, based on county population. This sample of 405 represents the universe of counties which have consistently defined mortality data from NCHS for the period 1993-2004.

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165. Exhibit 42 summarizes shipments of prescription opioids by county in Ohio for the 1997-2010 period, expressed as a ratio to the national level of shipments per capita over the same period. As this exhibit demonstrates, many counties in Ohio (including Trumbull County) received shipments at ratios above the national average. In particular, there are clusters of counties in southern Ohio, near the borders with Kentucky and West Virginia with very high shipments relative to the national average.

Exhibit 42

Shipments of Prescription Opioids by County: 1997-2010 Average Comparison to National Average



Source: ARCOS.

166. As discussed in Section III above, the explosive growth in shipments during the 1990s generated a recognition of growing opioid misuse and opioid-related mortality, which in turn generated responses by law enforcement officials, policymakers, and industry participants, both nationally and locally. Locally, Ohio established a Prescription Drug Monitoring Program in 2006 called the Ohio Automated Rx Reporting System (OARRS). Usage of OARRS by prescribers

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was mandated starting in 2011.¹³⁹ Additionally, the Ohio legislature enacted HB 93, a law intended to shut down “pill mill” pain clinics in May 2011. This legislation also expanded OARRS, limited prescribers’ ability to prescribe certain drugs, enhanced licensing and enforcement of pain-management clinics and developed a statewide prescription drug “take-back” program.¹⁴⁰

167. The policies enacted by law enforcement officials, industry participants, and policymakers had the desired effect of reducing shipments of prescription opioids. Shipments to Trumbull and Lake counties, and to Ohio and the U.S. overall, started to decline around 2010. Between 2010 and 2019, per capita shipments fell 55 percent in Trumbull County and 67 percent in Lake County. Nationally, shipments fell 53 percent over this period. Nevertheless, per capita shipments in 2019 in Trumbull County remained 242 percent higher than in 1997, the year after OxyContin was launched; shipments to Lake County in 2019 were 104 percent above the 1997 level.

C. Trends in Opioid Mortality in Trumbull and Lake Counties: 1993-2010

168. Exhibit 43 compares trends in total opioid mortality between 1999 and 2010 for Trumbull and Lake counties, Ohio, and the U.S. The year-to-year variation in mortality in individual counties is greater than the year-to-year variation observed in Ohio or the U.S., an unsurprising pattern because idiosyncratic local factors in any given area and time period tend to be offsetting in analysis based on larger geographic areas.

169. Exhibit 43 demonstrates that:

¹³⁹ See Ohio Automated Rx Reporting System, <https://www.ohiopmp.gov/About.aspx>; Laura A. Bischoff, “DeWine to drug makers: It’s time to reach a settlement,” *Dayton Daily News*, Aug. 2, 2019, <https://www.daytondailynews.com/news/dewine-drug-makers-time-reach-settlement/D1HPe22FzBaBKj37vPcNHJ/>.

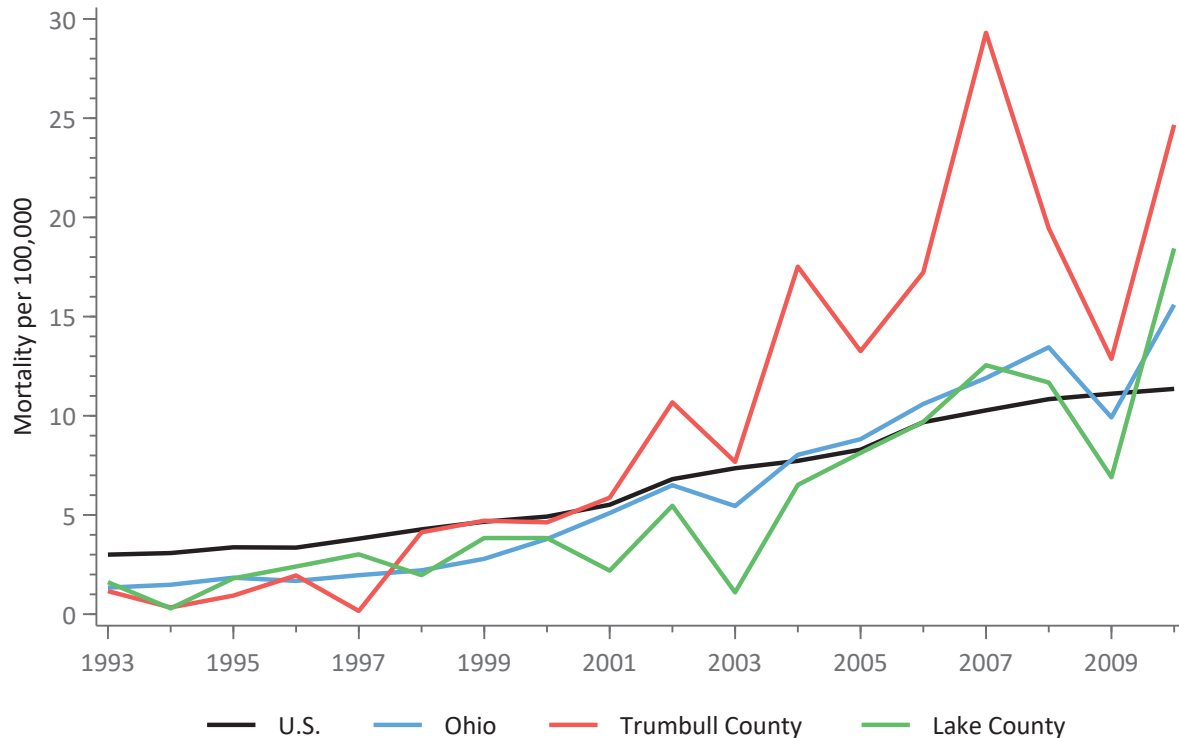
¹⁴⁰ See “Kasich signs ‘pill mill’ bill,” *The Columbus Dispatch*, May 21, 2011, <https://www.dispatch.com/article/20110521/NEWS/305219758>.

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- Trumbull County experienced greater increases in opioid mortality in this period compared to Lake County or the U.S. and Ohio averages. This is consistent with the higher level of shipments of prescription opioids to Trumbull between 1997-2010. Opioid mortality in Trumbull County was at or below the national average from 1993-2001 and after that exceeded the national average through 2010. Trumbull County ranked 42nd among the 405 counties in the large county sample for overall opioid mortality in 2010.
- Lake County was at or below the national average in opioid-related mortality through 2009 and rose above it in 2010. Lake County ranked 137th among counties in the large county sample for overall opioid mortality in 2010. The lower level of aggregate opioid mortality in Lake County relative to Trumbull is consistent with the lower level of shipments to the area over this period.

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Exhibit 43

Total Opioid Mortality Rates: 1993-2010
Ohio and U.S. Total

Source: NCHS Mortality Data and Census Data.

170. The growth in opioid mortality through 2010 in Trumbull and Lake counties is largely, but not fully, attributable to the growth of prescription opioid mortality. The left panel of Exhibit 44 shows that prescription opioid mortality increased substantially in both Trumbull and Lake counties during the 2000s. Trumbull County generally had higher prescription opioid mortality rates than those observed in Lake County or in Ohio as a whole. Prescription opioid mortality rates in Lake County were generally at or below the national average.

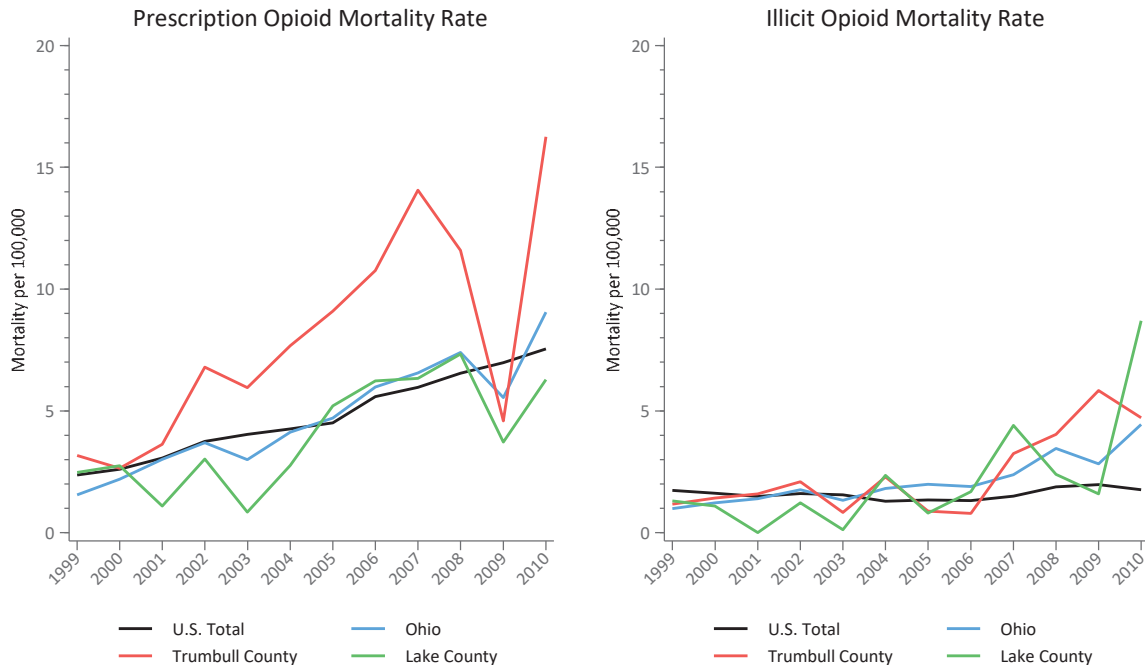
171. The right panel of Exhibit 44 reports illicit mortality rates in Lake and Trumbull counties during the 2000s, as well as trends for Ohio and the U.S. Prior to 2006, illicit opioid mortality in Trumbull and Lake counties did not follow any clear trend, but illicit opioid

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mortality in both areas started to grow after 2007 while the national average did not. Illicit opioid mortality for Ohio also grew relative to the national average after 2004.

Exhibit 44

Prescription vs. Illicit Opioid Mortality Rates: 1999-2010 Ohio and U.S. Total



Source: NCHS Mortality Data and Census Data.

172. The growth in illicit opioid mortality in Trumbull and Lake Counties that started in the mid-2000s reflects a combination of factors including: (i) the growth in the number of individuals dependent on opioids due to the growth in prior shipments; (ii) that some users of prescription opioids turned to illicit substitutes when prescription opioids were not available to them or became more difficult to obtain; and (ii) the widespread availability of heroin in the area prior to 2010. In this sense, Trumbull and Lake counties were a relatively small early warning sign for the much larger illicit crisis that emerged after 2010.

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173. Changing patterns of heroin use in Ohio, and in northeast Ohio in particular, were identified and linked to prescription opioid abuse as early as 2001 by the Ohio Substance Abuse Monitoring Network (OSAM). For example:

- In June 2001, OSAM noted that the “emerging population of new young heroin users continued in Dayton, Akron and Cleveland and was also reported in the OSAM Network areas of Youngstown and Toledo.”¹⁴¹
- OSAM undertook an investigation of the emerging heroin problem in the 2001-02 period, which “revealed an alarming trend—a connection between oxycodone long-acting (OxyContin) and heroin abuse. Young, new heroin abusers seeking treatment reported OxyContin abuse prior to becoming addicted to heroin. Several individuals reported resorting to heroin when their OxyContin habits became too expensive or when the drug became difficult to obtain. Abuse of OxyContin prior to the abuse of heroin appears to be a common pattern, especially among new, young, white heroin addicts.”¹⁴²
- In January 2002, OSAM noted that in “Dayton, Youngstown and Northeast Ohio, the abuse of OxyContin is reportedly increasing among the younger population—

¹⁴¹ OSAM-O-GRAM, “Heroin Abuse Among White, Suburban Youth and Young Adults Continues to Rise and Spreads to Other Areas in Ohio,” October 5, 2001, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2001-Jun-OSAM-O-Gram-Heroin.pdf>.

¹⁴² OSAM-O-GRAM, “OSAM Rapid Response Investigation Reveals Connection Between OxyContin Abuse and Heroin Addiction in Some Individuals,” January 24, 2002, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2002-Jan-OSAM-O-Gram-Connxts-Oxy.pdf>.

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many of whom have begun abusing heroin when they could no longer obtain or afford OxyContin®.”¹⁴³

- In January 2004, OSAM announced that they observed continuing increases in heroin abuse and availability throughout the state and noted that “[t]he relationship between initial abuse of pharmaceutical opioids, especially OxyContin (oxycodone controlled-release), and subsequent transition to heroin abuse continued to be reported by drug users and treatment providers in most reporting areas of the state.”¹⁴⁴
- The results of a youth heroin study released by OSAM in June 2006 noted that “[a]lmost 65 percent of the participants believed they were addicted to nonprescribed pharmaceutical opioids before trying heroin for the first time. About 70% of these participants reported that OxyContin was the pharmaceutical drug they most commonly abused before transitioning to heroin. Four interrelated factors contributed to their transition to heroin: 1) rapidly increasing tolerance to pharmaceutical opioids; 2) decreasing availability and high street prices of OxyContin; 3) high availability and comparatively low prices of heroin; and 4) a

¹⁴³ OSAM-O-GRAM, “OxyContin Abuse Continues to Increase and Spread Throughout Ohio,” January 24, 2002, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2002-Jan-OSAM-O-Gram-Oxy-Cont-OH-Increase.pdf>.

¹⁴⁴ OSAM-O-GRAM, “Increases in Heroin Availability and Abuse Continue to be Reported Across the State,” January 2004, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2004-Jan-OSAM-O-Gram-Heroin-Avail-Abuse.pdf>.

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commonly shared belief that heroin is the ‘same thing as OxyContin,’ which diminished stigma and initial fears associated with its use.”¹⁴⁵

D. Trends in Opioid Mortality in Trumbull and Lake Counties: 2010-19

174. As discussed in Section III above, the responses to the opioid crisis that were gradually enacted starting around 2008 locally and nationwide, including increased oversight of prescription activity, legal actions against manufacturers, distributors, and dispensers as well as the reformulation of Oxycontin, marked a critical turning point in the opioid epidemic. These reforms had the desired effects of reducing shipments of prescription opioids and reducing mortality from prescription opioids.

175. However, the reduction in the availability of prescription opioids unleashed a dramatic increase in illicit opioid use, opioid-related mortality, and related harms. These responses greatly accelerated the increase in illicit mortality observed since the mid-2000s. Trumbull and Lake counties, and Ohio more generally, were particularly hard hit by the illicit opioid crisis, and the increase in illicit opioid mortality after 2010 in these areas was far greater than the decline in mortality from prescription opioids.

176. Exhibit 45 documents the dramatic rise in total opioid mortality (including both prescription and illicit opioid mortality) in Trumbull and Lake counties as well as in Ohio and the U.S. after 2010. Between 2008-10 and 2018-19, the opioid mortality rate increased 165 percent in Trumbull County and 176 percent in Lake County, much higher than the 75 percent increase for the U.S.¹⁴⁶ In 2018-19, the opioid mortality rate was 159 percent above the

¹⁴⁵ OSAM-O-GRAM, “Targeted Response Initiative on Young Heroin Users in Ohio Part II: Initiation to Heroin Use,” June 2006, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2006-Jun-OSAM-O-Gram-Youth-Heroin-Usrs-Prt2.pdf>.

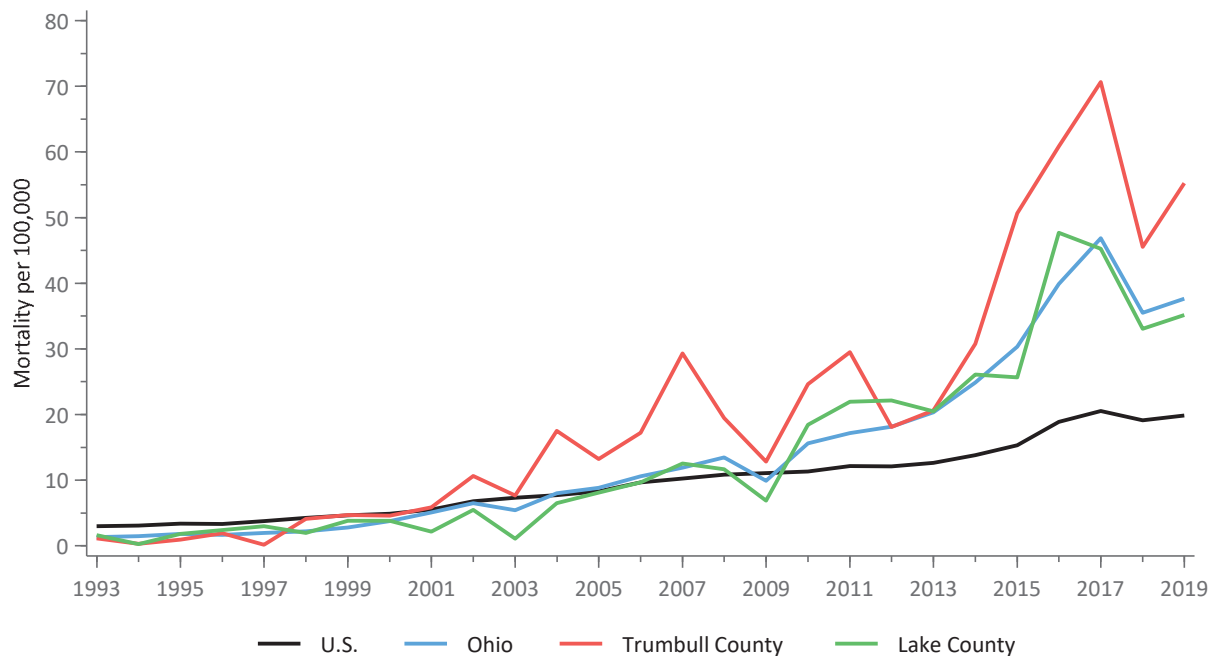
¹⁴⁶ Calculated from NCHS MCOD data.

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national average in Trumbull County; and 75 percent above the national average in Lake County. In 2018-19, Trumbull and Lake Counties respectively had the 22nd and 81st highest opioid mortality rates among the 405 large counties analyzed.¹⁴⁷

Exhibit 45

Total Opioid Mortality Rates: 1993-2019 Ohio and U.S. Total



Source: NCHS Mortality Data and Census Data.

177. Exhibit 46 separately documents separately the growth in prescription opioid mortality and illicit opioid mortality between 1993 and 2019.

- As shown in the left panel, between 2008-10 and 2018-19, prescription opioid mortality fell 39 percent for the U.S., 45 percent in Trumbull County and 30 percent in Lake County. Prescription mortality rates in both Trumbull and Lake counties were close to the national average.

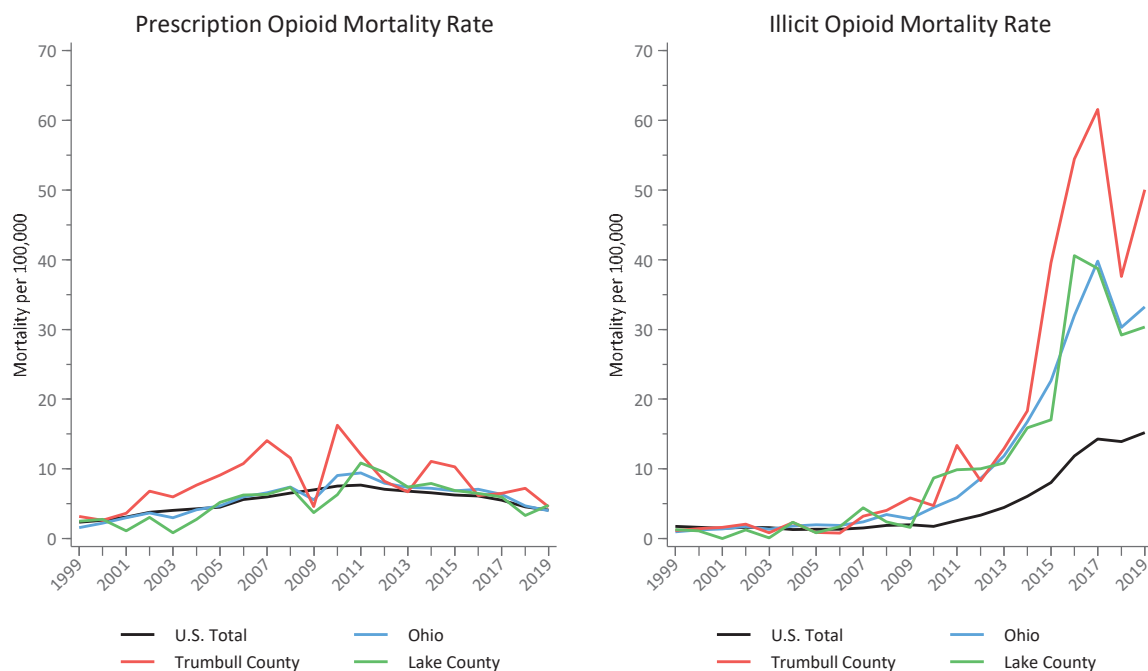
¹⁴⁷ Calculated from NCHS MCODE data.

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- As shown in the right panel, between 2008-10 and 2018-19, illicit opioid mortality grew far more rapidly in Trumbull and Lake counties, and in Ohio as a whole, relative to the national trend. Between 2008-10 and 2018-19, illicit opioid mortality grew 801 percent in Trumbull County and 603 percent in Lake County, compared to 676 for the U.S. By 2018-19, illicit mortality was triple the national average in Trumbull County and double the national average in Lake County. In 2018-19, Trumbull County had the 22nd highest illicit mortality rate among 405 counties in the national large county sample; Lake County ranked 74th.

Exhibit 46

Prescription vs. Illicit Opioid Mortality Rates: 1999-2019 Ohio and U.S. Total



Source: NCHS Mortality Data and Census Data.

178. Trumbull and Lake Counties are representative of a broader set of communities in Ohio and neighboring states that were particularly hard hit by the emergence of the illicit

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opioid crisis. As noted above, OSAM observed that heroin was readily available in the area prior to 2010. OSAM also observed that powdered heroin had been the predominant form of heroin available in the area at the time.¹⁴⁸ As described above in Section III above, powdered heroin is a closer substitute for (as well as a complement to) fentanyl than black tar heroin and areas where powdered heroin was more prevalent saw increased fentanyl mortality relative to areas with predominantly black tar heroin.

179. The increase in demand for illicit opioids after 2010, as well as the link between this demand and a decreased supply of prescription opioids, is well documented in OSAM reports from the period.¹⁴⁹ For example, an OSAM report from January through June 2011, around the start of the general decline in prescription opioid sales noted the following:

- In the Cleveland Region (which includes Lake County) OSAM noted that:
 “[e]vidence continues to show a progression from prescription opioid abuse to heroin abuse, earning the latter the reputation of being ‘one of the most available street drugs.’”¹⁵⁰
- In the Youngstown Region (which includes Trumbull County) OSAM noted that:
 “[t]reatment providers and law enforcement also most often reported heroin’s

¹⁴⁸ For example, the OSAM Report for the Cleveland Region (which includes Lake County) for June 2005 – January 2006 states “[p]articipants indicated continuing increases in heroin [] availability in the Cleveland area [] brownish powder was the most common form of heroin seen in the Cleveland area.” (OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio,” June 2005 – January 2006, p. 46) OSAM’s June 2008-January 2009 report for the Cleveland Region reported “[t]he Cleveland area crime lab reported overall high and stable heroin availability.” (OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio,” June 2008 – January 2009, p. 34) The OSAM report for the Youngstown Region (which includes Trumbull County) for June 2005 – January 2006 noted: “During this round, continued high availability of heroin [] was reported in Youngstown [] with brown powder as the most common form seen.” (OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio,” June 2005 – January 2006, p. 88) OSAM’s January 2008 – June 2008 report for the Youngstown Region reported “The availability of heroin in the Youngstown area was reported to be increasing.” (OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio,” January 2008 – June 2008, p. 68).

¹⁴⁹ This is an example of increases in demand for illicit opioids generating “thickness” in markets for heroin.

¹⁵⁰ OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio,” January 2011 – June 2011,” p. 62.

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current availability as ‘10.’ A law enforcement officer reported, ‘I don’t think there’s been a day out here when we said, ‘hey, we got a chance to buy heroin, and the deal has fallen through. It’s always available.’ A treatment provider reported, ‘Ten. It’s [heroin] the most available drug out there now, and, um, everyone’s using it, snorting it or shooting [injecting] it. And, they’re using heroin more because of the unavailability of the pills [prescription opioids] they used to seek, and because it is a lower cost, the heroin, and it goes a lot further.’”¹⁵¹

OSAM also notes that “[p]articipants attributed the increase in heroin over the past six months mostly to the price of prescription opioids: ‘The pills [prescription opioids], the OxyContin are harder to get; they’re harder to break down. They cost more money []’.”¹⁵²

- In the Akron region (which is adjacent to OSAM regions that include Trumbull and Lake counties) OSAM noted that: “Participants reported that overall availability of heroin has increased over the past six months. Participants stated, ‘Heroin [availability] has skyrocketed; Instead of my calling a few people to find it [heroin], they call me, they [dealers] come to me.’ Participants commonly cited that due to efforts to make intravenous use of prescription opioids more difficult (changing the formulation of OxyContin), heroin use and availability have increased: ‘Because they [Purdue Pharma] changed Oxy’s [OxyContin], pills [prescription opioids] are harder to get. People [users] are changing to heroin.’”¹⁵³

¹⁵¹ OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio, January 2011 – June 2011,” p. 128.

¹⁵² OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio, January 2011 – June 2011,” p. 128.

¹⁵³ OSAM, “Surveillance of Drug Abuse Trends in the State of Ohio, January 2011 – June 2011,” p. 14.

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180. OSAM reports from 2014 and later show the progression of illicit opioid use from heroin to fentanyl in Ohio. For example, in a September 2015 update, OSAM noted that “[u]sers, treatment providers and law enforcement from across Ohio reported that much of the heroin supply is adulterated with fentanyl and that fentanyl is often sold as heroin.”¹⁵⁴ The same report identified fentanyl-cut heroin in the Cleveland Region (which includes Lake County) as early as June 2011 and in the Youngstown Region (which includes Trumbull County) as early as January 2014.¹⁵⁵ Within a few years, users in Ohio were reporting to OSAM that they were seeking out fentanyl because it was stronger than heroin. For example, one OSAM participant noted:

“The heroin is cut with fentanyl and carfentanil; Everyone wants it if it’s cut with fentanyl because it is stronger ... and it’s even better ‘dope’ (heroin) if it’s mixed with carfentanil; If somebody overdoses and dies, they (users) want to know who provided that dope because it was obviously good; I never worry about overdosing. I overdosed one time ... it took me six shots of Narcan® (naloxone, medication to reverse opioid overdose) ... to get back; People are overdosing because of the fentanyl and carfentanil.”¹⁵⁶

181. The growth of illicit opioid markets after 2010 is also reflected NFLIS data on heroin and fentanyl seizures by law enforcement, which shows that Ohio has had the highest rate of heroin and fentanyl seizures per capita of any state in the U.S. since 2015. The state has ranked in the top 10 in terms of heroin and fentanyl seizures per capita since at least 2007, the earliest year for which data are available. Exhibit 47 summarizes data from NFLIS on the share

¹⁵⁴ OSAM-O-GRAM, “Much of Heroin Supply Adulterated with Fentanyl,” September 2015, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2015-Sep-OSAM-O-Gram-Heroin-Fentanyl-Update.pdf>.

¹⁵⁵ OSAM-O-GRAM, “Much of Heroin Supply Adulterated with Fentanyl,” September 2015, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2015-Sep-OSAM-O-Gram-Heroin-Fentanyl-Update.pdf>.

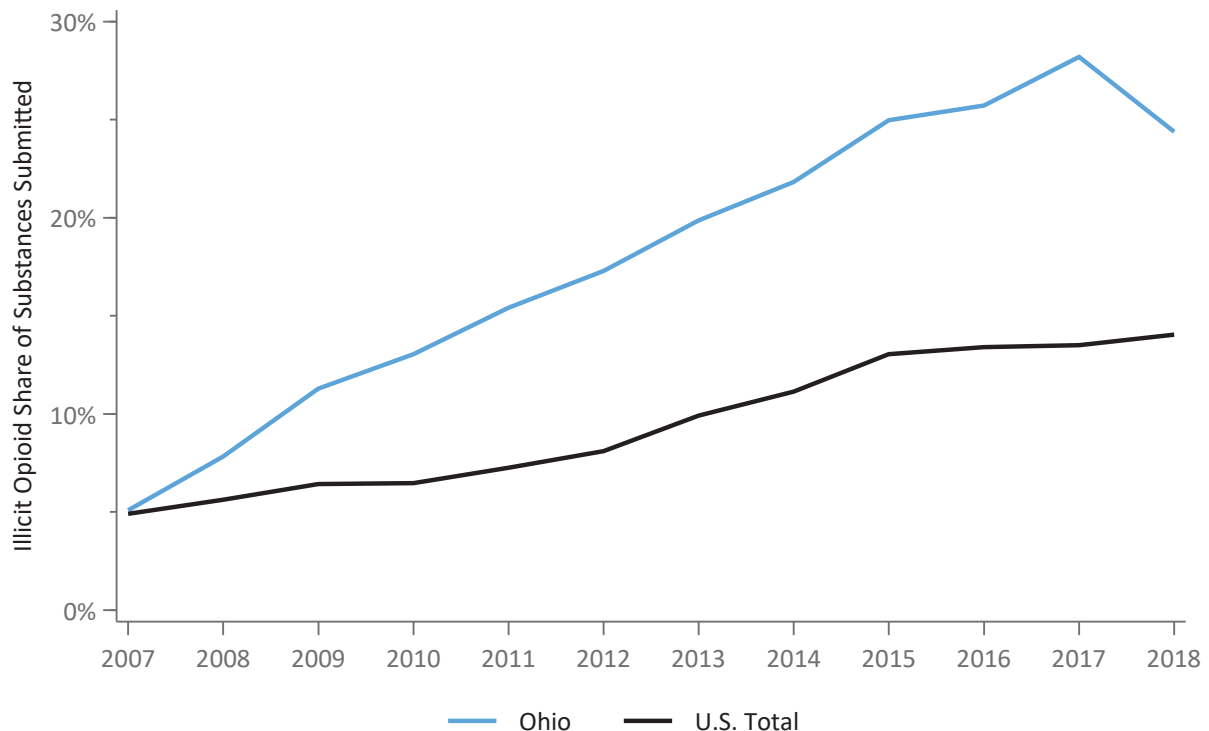
¹⁵⁶ OSAM-O-GRAM, “Fentanyl and the Deadlier Carfentanil, Now Outpacing Heroin Sales in Many Areas,” March 2017, available at <https://mha.ohio.gov/Portals/0/assets/ResearchersAndMedia/Workgroups%20and%20Networks/OSAM/OSAM-O-Grams/2017-Mar-OSAM-O-Gram-Fentanyl-Carfentanil.pdf>.

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of confiscations of illegal drugs by law enforcement that involved heroin or fentanyl. The exhibit shows that confiscations of illicit opioids as a share of total confiscations was approximately 5 percent for both the U.S. and Ohio in 2007, but that by 2010 this share increased to 13 percent in Ohio but to only 7 percent nationally. By 2017, the share for Ohio was 28 percent, compared to 16 percent nationally.

Exhibit 47

Share of Drug Confiscations Involving Illicit Opioids Ohio and U.S. Total



Source: U.S. Drug Enforcement Administration, Diversion Control Division.

182. As discussed in Chapter 1, increases in the demand for heroin and later fentanyl after 2010 resulted in a thicker market for illicit drugs that contributed to increased abuse of other drugs other than opioids. More specifically, the DEA recognizes that transnational criminal organizations control most of the drug market in the United States, producing and

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distributing heroin, fentanyl, cocaine, methamphetamines, and marijuana as well illicit activities unrelated to drugs. The OSAM reports for Ohio document how the market for illicit opioids expands to increase the use of other drugs.

183. OSAM reports in 2017 documented statewide increases in methamphetamine use linked to heroin sales:¹⁵⁷

“During the past six months, we’ve seized more than 20 pounds of meth; The Mexican groups are using the heroin distributors to set up the meth. Because they have so much of it ... they are offering it very cheap to try to get people to start buying it; When you get the established heroin customer and you need two kilos of heroin, and they’re sitting on a pile of meth, then they say, ‘I’ll send you two kilos of heroin but you’ll have to take two pounds of meth with it.’ They’re forcing it that way to try to create the market for meth; In order to get rid of their inventory in Mexico, they are forcing it on the people who want heroin.”

“Respondents noted that many meth users are heroin addicts and explained that the drug is often used to avoid opiate withdrawal symptoms. Meth is also used in combination with heroin for the ‘speedball’ effect (concurrent or consecutive stimulant and sedative highs).”

“It has definitely increased. We have more clients who have used meth, especially when they can’t get heroin; Half the intakes I did, they were doing meth; I’ve noticed in the past six months, my guys that used to do opiates are clean from that and are using meth; A lot of people on Vivitrol® are substituting [their opiate of choice] with meth.”

184. An OSAM report in 2018 documented that fentanyl increasingly was being used to cut other drugs:¹⁵⁸

“[T]he Ohio Department of Health has issued an advisory on the increase in fentanyl-related overdose deaths involving non-opioids, such as cocaine and methamphetamine. This advisory urges first-responders to administer naloxone for all drug overdoses, even when non-opioids are suspected. Several local health departments have issued similar advisories. On January 17, 2018, Columbus Public Health sent out a press release alerting the public to an increase in overdose deaths where both cocaine and fentanyl were contributors. The release also cautioned the public that fentanyl can be found in any street drug. Since OSAM’s

¹⁵⁷ OSAM, “Statewide Increases in Methamphetamine Linked to Heroin,” March 2017.

¹⁵⁸ OSAM, “Increase in Fentanyl-Cut Drugs,” March 2018.

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reporting of June 2015 drug trends, participants throughout OSAM regions have reported fentanyl as a top cutting agent (adulterant) for heroin. OSAM's first report of fentanyl as a cut for a non-opioid was in January 2017 when participants in Toledo and Youngstown reported fentanyl as a cut for powdered cocaine, and a law enforcement officer in Youngstown commented, 'They're cutting cocaine with fentanyl, too.' Fentanyl is now believed to be cut into many drugs.

In the same report, OSAM reported the following table summarizing the growth over time in the use of fentanyl as a cutting agent.

Table 1. Drugs cut with fentanyl as reported by OSAM respondents per reporting period^a.

January 2017 Report (June 2016 – January 2017)	June 2017 Report (January – June 2017)	January 2018 Report^b (June 2017 – January 2018)
Heroin Powdered cocaine	Heroin Powdered cocaine Crack cocaine Prescription opioids^c Sedative-hypnotics^c Marijuana Methamphetamine Molly (powdered MDMA)	Heroin Powdered cocaine Crack cocaine Prescription opioids Sedative-hypnotics Marijuana Methamphetamine Molly (powdered MDMA) Ecstasy

^aReports may be accessed here: <http://mha.ohio.gov/research/osam>.

^bPreliminary data: OSAM's January 2018 Drug Trend Report will be ready for release in June 2018.

^cFentanyl is pressed into pills resembling prescribed medications (e.g., Percocet[®] and Xanax[®]).

185. Exhibit 48 summarizes trends in shipments, total opioid mortality, prescription opioid mortality, and illicit opioid mortality in Trumbull and Lake counties, Ohio, and the U.S. As the table shows, Trumbull County, and to a lesser extent, Lake County are stark examples of how the prescription opioid crisis morphed into an even larger illicit opioid crisis. Trumbull and Lake counties, like much of the rest of Ohio, received shipments of prescription opioids roughly consistent with national averages through 2010 and saw increases in prescription opioid mortality through 2010, consistent with the national trends. However, Lake and Trumbull counties and surrounding areas were characterized by ready availability of powdered heroin, which many individuals turned to as a substitute as supplies of prescription opioids were restricted. The increases in demand for illicit opioids, in turn, incentivized further increases in

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the supply of illicit opioids through the existing distribution chain. The result in Trumbull and Lake counties, and many other areas in Ohio and the U.S., was an illicit crisis far more deadly than the one initially caused by the large increases in shipments of prescription opioids over the prior 20 years.

Exhibit 48
Shipments and Illicit and Total Opioid Mortality:
U.S. and Ohio

Region	Shipments					
	MME Per Capita Per Day			% Change		
	1997	2010	2019	1997-2010	2010-2019	1997-2019
U.S. Total	0.43	2.47	1.16	469%	-53%	168%
Ohio	0.45	2.91	1.04	552%	-64%	133%
Lake County	0.33	2.05	0.67	525%	-67%	104%
Trumbull County	0.37	2.84	1.27	666%	-55%	242%

Region	Mortality					
	Prescription Mortality Rate			% Change		
	1999	2010	2019	1999-2010	2010-2019	1999-2019
U.S. Total	2.37	7.54	4.09	218%	-46%	72%
Ohio	1.56	9.06	3.98	481%	-56%	155%
Lake County	2.47	6.28	4.80	154%	-24%	94%
Trumbull County	3.16	16.25	4.56	414%	-72%	44%

Region	Illicit Opioid Mortality			% Change		
	1999	2010	2019	1999-2010	2010-2019	1997-2019
	1999	2010	2019	1999-2010	2010-2019	1997-2019
U.S. Total	1.73	1.77	15.22	2%	759%	778%
Ohio	1.00	4.45	33.24	347%	647%	3240%
Lake County	1.31	8.71	30.36	565%	249%	2218%
Trumbull County	1.17	4.72	50.04	304%	961%	4186%

Region	Total Opioid Mortality			% Change		
	1999	2010	2019	1999-2010	2010-2019	1997-2019
	1999	2010	2019	1999-2010	2010-2019	1997-2019
U.S. Total	4.67	11.35	19.84	143%	75%	325%
Ohio	2.79	15.60	37.66	459%	141%	1251%
Lake County	3.85	18.43	35.16	379%	91%	814%
Trumbull County	4.70	24.66	55.25	424%	124%	1075%

Note: Mortality is measured as opioid overdose mortality rate per 100,000 population.

Sources: NCHS Mortality Data and ARCOS.

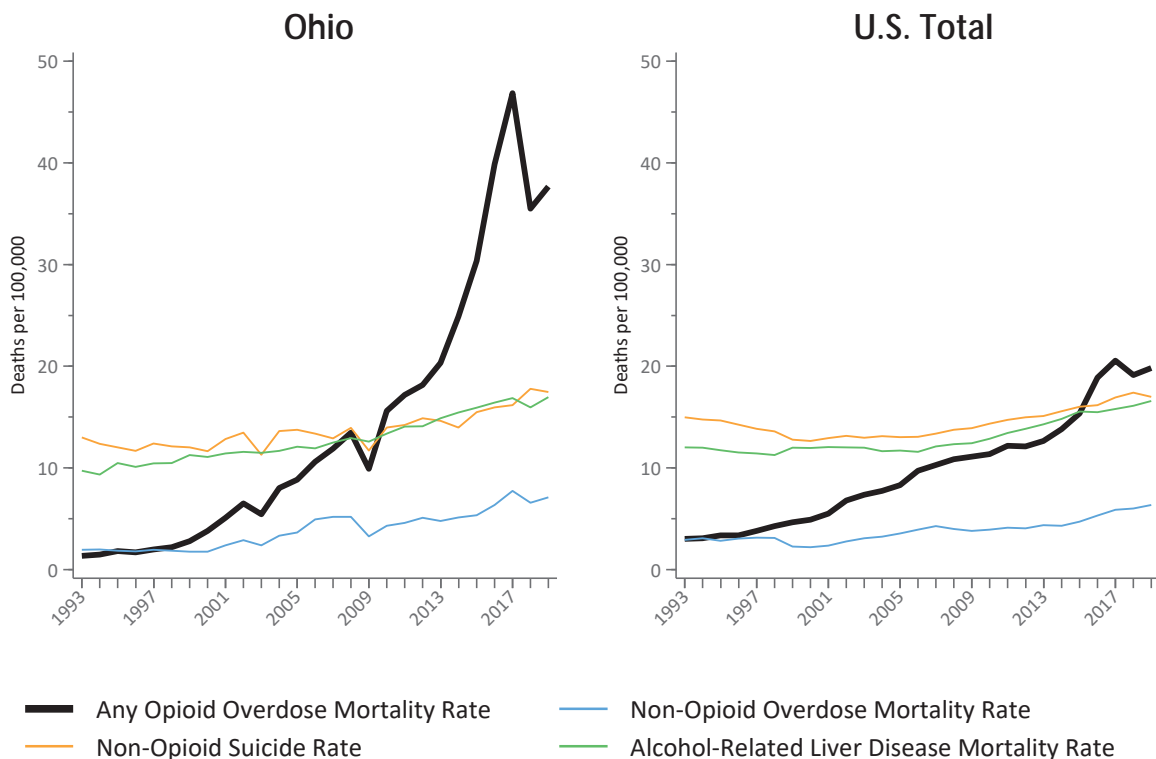
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E. Trends in "Demand Side" Factors Affecting Mortality in Ohio

186. As discussed in Section VI above, some analysts have argued that that "demand side" factors, such as depression, despair, and increasing social isolation have driven a range of "deaths of despair," including opioid mortality. My analysis in Section VI showed that trends in opioid-mortality deaths were distinct from trends in non-opioid drug overdoses, suicides, and alcohol-related liver diseases (which are associated with alcoholism). Exhibit 49 compares trends in each of these types of mortality for Ohio and the U.S.

Exhibit 49

"Deaths of Despair" Mortality Rates: 1993-2019



Source: NCHS Mortality Data and Census Data.

187. As the exhibit indicates, opioid-related mortality grew far more rapidly than other metrics of deaths of despair in Ohio as well as in the U.S. since 1993. This provides

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further confirmation that the factors driving opioid-related mortality in Ohio differ from those affecting other types of deaths of despair.

IX. The Impact of Pharmacy Defendants' Misconduct on Opioid-Related Mortality in Trumbull and Lake Counties

188. The analysis of the impact of opioid shipments on mortality presented in Section IV above can be combined with estimates by James E. Rafalski, Carmen A. Catizone, and Dr. Craig McCann to estimate the extent to which opioid-related mortality in Trumbull and Lake counties is attributable to the misconduct of pharmacy defendants in CT3.¹⁵⁹ Dr. McCann's analyses identify the share of MMEs in each county that should have been investigated and cleared by defendants before dispensing or shipping based on the opinions of Mr. Rafalski and Mr. Catizone, respectively. I refer to these as "suspicious" shipments. My regression analyses establish the relationship between the level of MMEs in a county and the change in opioid-related mortality. This analysis yields an estimate of the opioid mortality expected in 2009-10 had shipments of prescription opioids remained at 1997 levels.

189. My analysis also established that the illicit opioid crisis was attributable to shipments of prescription opioids. The indirect analysis discussed in Section IV above estimates the level of opioid mortality in 2011-19 expected in the absence of patterns of opioid mortality observed in 2009-10. These estimates reflect the elevation in opioid mortality in 2009-10 due to earlier shipments, but not the impact of the illicit opioid crisis after 2010. Exhibit 50 summarizes the results of the indirect analysis for Trumbull and Lake counties, based on the regression results reported in Appendix 7, Table 2. The analysis indicates that, in the absence of the illicit crisis, changes in the economic and demographic characteristics of Trumbull and

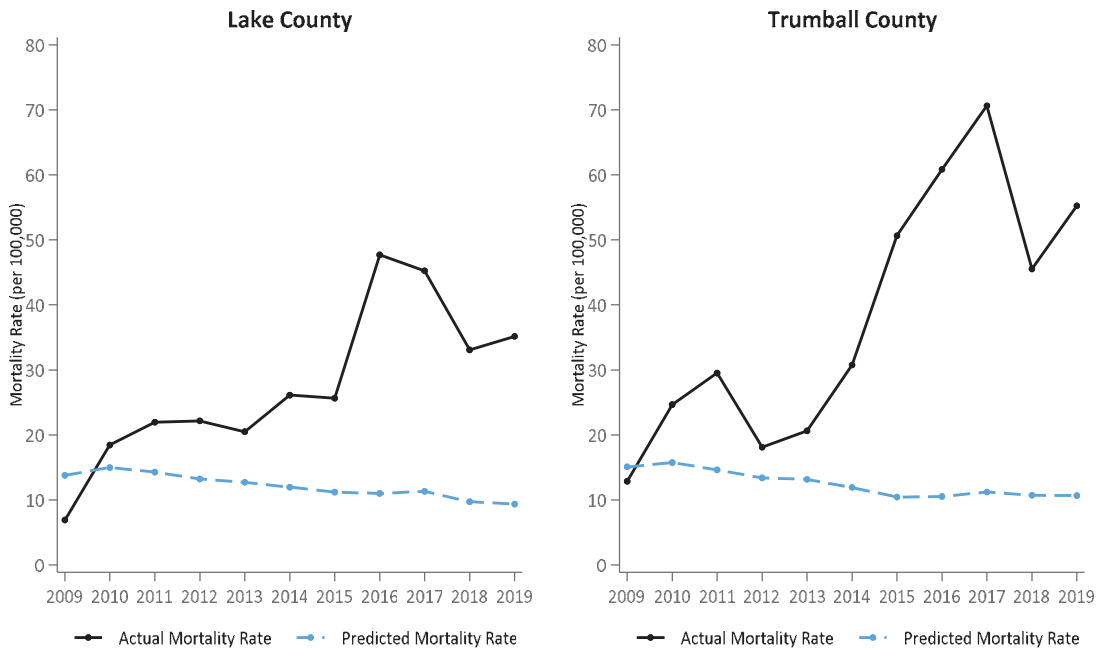
¹⁵⁹ Expert Report of James E. Rafalski, April 16, 2021 (hereafter "Rafalski Report"); Expert Report of Carmen A. Catizone, MS, RPh, DPh, April 16, 2021 (hereafter "Catizone Report") and Expert Report of Craig J. McCann, PH.D, CFA, April 16, 2021 (hereafter "McCann Report").

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Lake counties after 2010 would have been expected to result in a decline in opioid mortality rates. Instead, mortality rates increased dramatically in both areas.

Exhibit 50

**Actual and Predicted Opioid Mortality Rates in 2009-19
Based on Determinants of Opioid Mortality in 2009-10**



190. Together, these analyses can be used to estimate the level of opioid mortality expected in the absence of increases in shipments in prescription opioids since 1997. Combined with estimates by Mr. Rafalski, Mr. Catizone, and Dr. McCann of the share of shipments in Trumbull and Lake counties that defendants should have identified, investigated and cleared before dispensing or shipping, the analysis can be used to estimate the increase in opioid-related mortality (and the number of deaths) in Trumbull and Lake counties in 2009-10 attributable to defendants' misconduct.

191. I calculate the impact of defendants' misconduct on opioid-mortality under three scenarios evaluated by Mr. Rafalski, Mr. Catizone, and Dr. McCann that estimate the share of all

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MMEs sold in Trumbull and Lake Counties between 2006-10 that defendants should have identified as suspicious, in each defendant's capacity as either dispensers or distributors.¹⁶⁰ The first two scenarios evaluate MMEs that defendants should have identified as suspicious in their role as dispensers of prescription opioids based on the opinions of Mr. Catizone, as implemented by Dr. McCann. The third scenario evaluates the share of MMEs that defendants should have identified as suspicious in their role as distributors, based on the opinions of Mr. Rafalski, as implemented by Dr. McCann.

- Scenario 1 reflects estimates of the share of MMEs that defendants should have identified as suspicious in their role as dispensers, as reported in Section X of Dr. McCann's report.¹⁶¹
- Scenario 2 reflects estimates of the share of MMEs that defendants should have identified as suspicious in their role as dispensers under the same criteria also including as suspicious all subsequent prescriptions dispensed to the same patient and/or written by the same prescriber, as reported in Section X of Dr. McCann's report.¹⁶²
- Scenario 3 reflects estimates of the share of MMEs that defendants should have identified as suspicious in their role as distributors, as identified by the "Method 1" criteria as reported in Section VII of Dr. McCann's report. This approach identifies transactions in which shipments to a pharmacy by a defendant in their role as a

¹⁶⁰ I understand that Dr. McCann's calculations may be revised, in which case the calculations presented in this section would be revised. Consistent with paragraph 7 above, I reserve the right to supplement my calculations based on the final numbers provided by Dr. McCann in his report. The calculations provided to me by Dr. McCann have no impact and do not otherwise change the methodology for evaluating the impact of the pharmacy defendants' misconduct on opioid-related mortality in Lake and Trumbull Counties.

¹⁶¹ See McCann Report, Section X.C and related appendices.

¹⁶² See McCann Report, Section X.B and related appendices.

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distributor exceed shipments to the pharmacy in any one of the six preceding calendar months.¹⁶³

192. Dr. McCann estimates that in their role as dispensers, defendants together accounted for 48 percent of MMEs dispensed in Trumbull County and 59 of MMEs dispensed in Lake County between 2006-10.¹⁶⁴ Dr. McCann estimates that in their role as distributors, defendants together accounted for 17 percent of MMEs sold in Trumbull County and 36 of MMEs sold in Lake County between 2006-10. He estimates that between 2006-10, 39 percent of total MMEs in Trumbull County should have been identified as suspicious under Scenario 1, 96 percent under Scenario 2, and 69 percent under Scenario 3. Over the same period in Lake County, he estimates that 37 percent should have been identified as suspicious under Scenario 1, 94 percent under Scenario 2, and 69 percent under Scenario 3.

193. As noted, the analysis of Mr. Rafalski, Mr. Catizone, and Dr. McMann, together with my analysis of the impact of shipments of prescription opioids on mortality, yields estimates of the number of deaths attributable to defendants' misconduct. Exhibit 51 and 52 summarize this calculation using based on the Scenario 2 analysis. Exhibit 51 describes how these results together yield estimates of deaths attributable to defendant misconduct in 2009-10 and 2018-19. Exhibit 52 summarizes how this analysis is used to estimate estimates for other years.

¹⁶³ See McCann Report, Section VII.A. Shipments in Dr. McCann's distributor analysis are defined as dosage units, which typically reflect tablets or capsules.

¹⁶⁴ Dr. McCann estimates that in their role as distributors, defendants together accounted for 36 percent of MMEs distributed in Lake County and 17 percent of MMEs distributed in Trumbull County between 2006-10.

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Exhibit 51

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019
Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (2006-2010)	a	59%	48%
Flagged Percent of Defendants' MME (2006-2010)	b	94%	96%
Defendants' Flagged MMEs as Percent of Total	$c=a*b$	55%	46%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	d	12.68	18.75
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	e	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	$f=d-e$	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	$g=f*c$	2.47	2.89
Percent of Mortality Rate in 2009-2010 Attributable to Defendants	$h=g/d$	20%	15%
County Adult Population in 2009-2010	i	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	$j=g*(i/100,000)$	4.7	5.0
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	k	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	l	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	$m=k-l$	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	$n=m*c$	14.58	16.81
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	$o=f+m$	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	$p=g+n$	17.05	19.70
Percent of 2018-19 Mortality Rate Attributable to Defendants	$q=p/k$	50%	39%
County Adult Population in 2018-2019	r	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	$s=p*(r/100,000)$	32.9	32.5

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section X.B and Appendix 12.
Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

194. Estimates of opioid mortality attributable to defendants' misconduct in 2009-10 and 2018-19 involve the following steps:

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- The regression analysis reported in Appendix 9 Table 1 establishes the estimated magnitude of the relationship across counties between (i) shipments of prescription opioids (measured in MMEs per capita per day) between 1997-2010 and (ii) the change in mortality rates between 1993-95 and 2009-10. The regression model yields a prediction of county-specific average annual opioid mortality expected in the absence of any shipments of prescription opioids in 2009-10 (row e).
- Comparison of actual county-specific mortality (row d) yields an estimate of the increase in the opioid mortality rate attributable to all shipments (row f). Under Scenario 2, 55 percent of total MMEs in Lake County (and 46 percent in Trumbull County) should have been flagged as suspicious by defendants (row c), so I assume that defendants account for 55 percent of the increase in mortality estimated to be attributable to shipments of prescription opioids in Lake County (and 46 percent in Trumbull County). Together, these results imply that defendants' misconduct raised the average annual opioid mortality rate in 2009-10 by 2.47 per 100,000 in Lake County and 2.89 per 100,000 in Trumbull County (row g). Based on area population, this translates to an annual average of 4.7 deaths in Lake County and 5.0 deaths in Trumbull County in 2009-10 that are attributable to defendants' misconduct.
- The county-specific estimate of opioid overdose rates in Trumbull and Lake counties expected in the absence of the illicit crisis in 2018-19 is based on the "indirect" analysis, as summarized in Exhibit 50 above. The expected mortality rates as of 2018-19 based on this approach are reported in row I of Exhibit 51. The

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difference between (i) the actual mortality in 2018-2019 (row k); and (ii) expected mortality (row l) reflects the elevation in the opioid mortality rate between 2009-10 and 2018-19 due to shipments of prescription opioids (and is reported in row m).

- I again attribute 55 percent of the incremental mortality in 2018-19 in Lake County (and 46 percent in Trumbull County) to defendants' misconduct based on the Scenario 2 analysis, as reflect in row c. The resulting estimate of the incremental annual mortality rate in 2018-2019 that is attributable to defendants: 14.58 deaths per 100,000 in Lake County and 16.81 deaths per 100,000 in Trumbull County (as reported in row n).
- The overall average annual impact of the defendants' misconduct in 2018-19 is calculated as the sum of the estimates of the impact of defendants' misconduct in 2009-10 and 2018-19. Together, these results indicate that defendants' misconduct elevated the opioid mortality rate by 17.05 deaths per 100,000 residents in Lake County and by 19.70 deaths per 100,000 residents in Trumbull County (row p). This in turn implies that in 2018-19, defendants' misconduct resulted in an average of 32.9 deaths per year in Lake County and 32.5 deaths per year in Trumbull County (row q).

195. Exhibit 52 extends this analysis to determine the level of mortality that is attributable to defendants' misconduct for intervening years. Within each period, I determine the percent of mortality that is attributable to defendants (columns b and f) under the assumption that this percentage grew at the same amount per year between 1993-95 and 2009-10 and then between 2009-10 and 2018-19. In Lake County, for example, the percent of

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mortality attributable to defendants increases from 0 in 1993-95 to 20 percent in 2009-10. For the years in between these two points, the percentage is assumed to increase by the same amount per year. This assumption is favorable to defendants in that it assumes the impact of their misconduct was gradual; an alternative approach would assume that the 20 percent elevation in mortality determined as of 2009-10 applies to all years in which defendants failed to prevent suspicious sales and would generate higher levels of mortality attributable to that misconduct.

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Exhibit 52

Impact of Defendants on Annual Total Opioid Mortality By Year
Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	1%	0.03	0.1	1.95	1%	0.02	0.0
1997	3.01	3%	0.08	0.2	0.17	2%	0.00	0.0
1998	1.97	4%	0.08	0.1	4.13	3%	0.14	0.2
1999	3.85	6%	0.21	0.4	4.70	4%	0.21	0.4
2000	3.84	7%	0.27	0.5	4.62	6%	0.25	0.5
2001	2.19	8%	0.18	0.3	5.87	7%	0.39	0.7
2002	5.47	10%	0.53	1.0	10.68	8%	0.82	1.5
2003	1.09	11%	0.12	0.2	7.68	9%	0.68	1.2
2004	6.52	13%	0.82	1.5	17.52	10%	1.74	3.1
2005	8.13	14%	1.13	2.1	13.25	11%	1.46	2.6
2006	9.70	15%	1.49	2.8	17.22	12%	2.09	3.7
2007	12.55	17%	2.10	3.9	29.30	13%	3.87	6.8
2008	11.68	18%	2.12	4.0	19.46	14%	2.78	4.8
Avg. 2009-2010	12.68	20%	2.47	4.7	18.75	15%	2.89	5.0
2011	21.96	23%	5.12	9.7	29.51	18%	5.42	9.3
2012	22.17	27%	6.01	11.4	18.09	21%	3.86	6.6
2013	20.49	31%	6.34	12.1	20.62	24%	5.01	8.5
2014	26.11	35%	9.07	17.3	30.75	27%	8.38	14.2
2015	25.65	39%	9.89	18.9	50.64	30%	15.30	25.8
2016	47.70	42%	20.21	38.7	60.86	33%	20.19	33.9
2017	45.25	46%	20.90	40.2	70.64	36%	25.52	42.5
Avg. 2018-2019	34.12	50%	17.05	32.9	50.39	39%	19.70	32.5
Total Deaths Attributable to Defendants (1996-2019)				240.4				

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section X.B and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

196. Overall, the results for Scenario 2 indicate that 240.4 deaths in Trumbull County and 241.4 deaths in Lake County were attributable to defendants' misconduct for 1996 through

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2019. Results of this analysis for Scenarios 1-3 are summarized in Exhibit 53.¹⁶⁵ The detailed results for each these calculations are presented in Appendix 12.¹⁶⁶

Exhibit 53
Impact of Defendants on Annual Total Opioid Mortality
Total Number of Deaths Attributable to Defendants, 1996-2019

Scenario	Approach	County	
		Lake County	Trumbull County
1	Dispenser Analysis, Non-Recurrent, 2006-2010 [1]	94.5	98.1
2	Dispenser Analysis, Recurrent, 2006-2010 [2]	240.4	241.4
3	Distributor Analysis, 2006-2010 [3]	108.1	59.4

Notes:

[1] Flagged MMEs based on 2006-2010 MMEs per McCann Section X.C and Appendix 12.

[2] Flagged MMEs based on 2006-2010 MMEs per McCann Section X.B and Appendix 12.

[3] Flagged MMEs based on 2006-2010 MMEs per McCann Section VII.A.

197. The estimates summarized in Exhibit 53, while substantial, are likely to understate, perhaps materially, the impact of defendants' misconduct on opioid mortality. As discussed above, the regression analysis relates MME shipments to changes in opioid mortality over time and treats all MME as equal. This is a simplification necessitated by the limitations of available data, which do not identify factors such as MMEs sold in high dose or long-term prescriptions which are more likely than other prescriptions to contribute to dependence and abuse. These types of measurement errors systematically reduce estimates of the impact of shipments on mortality.

¹⁶⁵ As noted above, these estimates reflect the assumption that the share of total area MMEs that defendants should have flagged in 1997-2005 is equal to that calculated by Rafalski/Catizone/McCann for 2006-10. As a check on the sensitivity of the results to that assumption, I have also estimated the number of deaths attributable to defendants' misconduct under the assumption that defendants' share of area MMEs that defendants should have flagged as suspicious in 1997-2005 is 50 percent of the level estimated for 2006-10. These results, which are presented in Appendix 13, are an average of 22 percent lower than the levels reported in Exhibit 53.

¹⁶⁶ Rafalski/Catizone/McCann report the share of MMEs that should have been identified as suspicious under additional scenarios for both dispensers and distributors. These can be evaluated directly based on the methodology described here and the data and programs produced with this report and Dr. McCann's.

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198. Perhaps more importantly, it is likely the diverted prescriptions that defendants failed to identify and stop result in a higher level of mortality and other harms than prescriptions that did not raise “red flags” because the diverted prescriptions were consumed for non-medical reasons. For example, as discussed in Section III.A of Chapter 1, 2010 NSDUH data indicate that only 19 percent of individuals that misused prescription opioids in the prior year obtained them from a doctor.

X. Trends in Other Opioid Related Harms in Ohio

199. While mortality is perhaps the most important opioid-related harm, as discussed in Section V above, shipments of prescription opioids have also resulted other harms, including increases in OUD, HUD, NAS, opioid-related emergency department visits and opioid-related hospital inpatient admissions, and increased placements of children in foster care. This section compares trends in these opioid-related harms in Ohio relative to the U.S. and confirms that shipments have indeed resulted in other harms. The analysis is based on statewide data because county-specific data that can be compared to data from other counties are not readily available.

- ***OUD/HUD***

200. Exhibit 54 summarizes estimates from NSDUH of opioid misuse and opioid-related disorders in 2006-09, the years preceding the onset of the increase in illicit mortality, and 2015-18, the most recent data available. The table reports four-year averages to reduce the impact of year-to-year variations that can result from the relatively small size of the NSDUH state-level samples. These data indicate that 0.85 percent of Ohio residents ages 12 and above had OUD in 2006-09, slightly higher than the U.S. rate of 0.77.¹⁶⁷ In 2015-18, 1.13 percent of

¹⁶⁷ Substance Abuse & Mental Health Data Archive’s Public-use Data Analysis System (PDAS). (<https://pdas.samhsa.gov/#/>)

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the population of Ohio population had OUD, compared to 0.80 percent of the U.S. population.

As discussed above, many analysts have concluded that NSDUH understates, perhaps dramatically, the number of if individuals with opioid use disorders.

201. The share of OUD estimated by NSDUH attributable to HUD also increased substantially over this period. In Ohio, HUD's share of OUD increased from 8.6 percent to 31.8 percent between 2006-09 to 2015-18. This growth is substantially larger than that for the U.S. over the same period, which increased from 15.6 percent to 27.7 percent.

Exhibit 54
Measures of Opioid-Related Disorder
U.S. vs. Ohio

	United States			Ohio		
	2006-2009	2015-2018	% Change	2006-2009	2015-2018	% Change
Heroin Use Disorder	0.12%	0.22%	84%	0.07%	0.36%	388%
RX Use Disorder	0.69%	0.66%	-5%	0.82%	0.89%	9%
Opioid Use Disorder	0.77%	0.80%	3%	0.85%	1.13%	33%
Heroin Share of OUD	15.61%	27.73%	78%	8.64%	31.82%	268%

Note: 4-year NSDUH averages used to reduce state-level variation due to small sample size.

2006-2009 Opioid UD defined as those with either Heroin or RX UD.

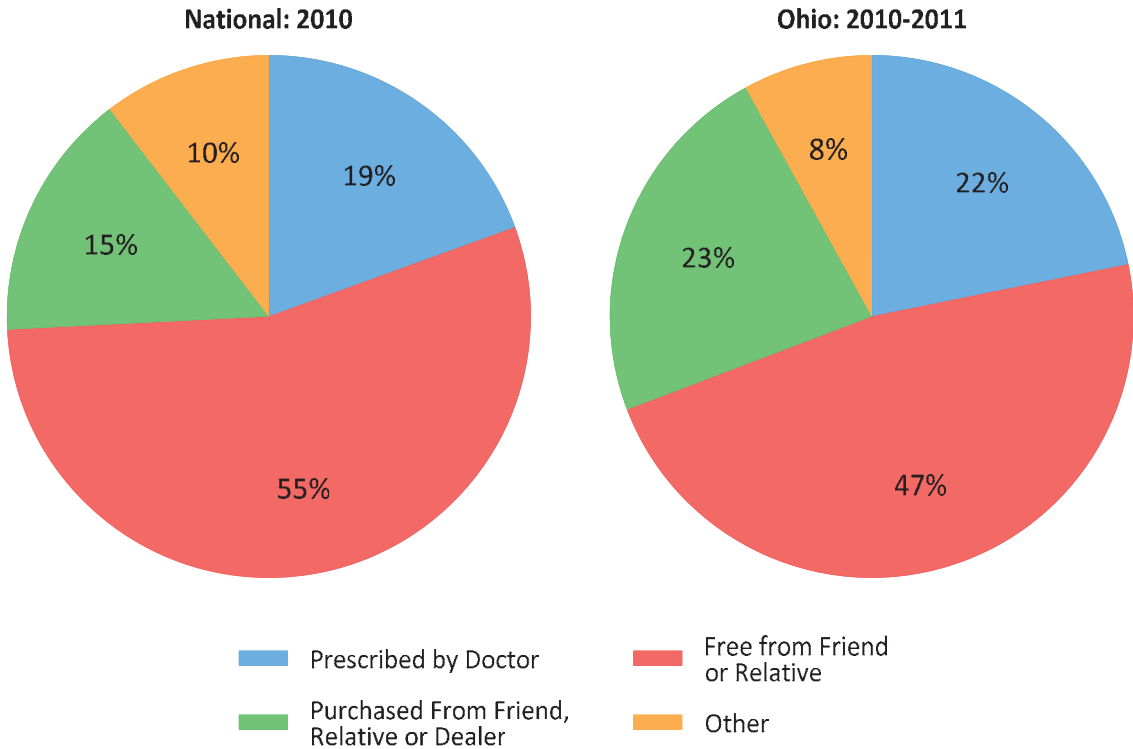
Source: NSDUH Restricted-use Data Analysis System.

202. The NSDUH data also establish that diversion of prescription opioids for non-medical use was widespread in Ohio, as it was for the U.S., around the start of the illicit opioid crisis. As shown in Exhibit 55 only 22 percent of Ohio residents that misused opioids obtained them from through a prescription. The comparable figure for the U.S. was 19 percent. The vast majority obtained them from for free from a friend or relative, or purchased them from a drug dealer, friend, or relative. This confirms that diversion of prescription opioids in Ohio for uses unrelated to medical need was widespread in Ohio at the start of the illicit crisis.

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Exhibit 55

**NSDUH Survey Data Indicate that Most Recent Pain Reliever Misuse is
Diversion from Friend, Relative, or Dealer**



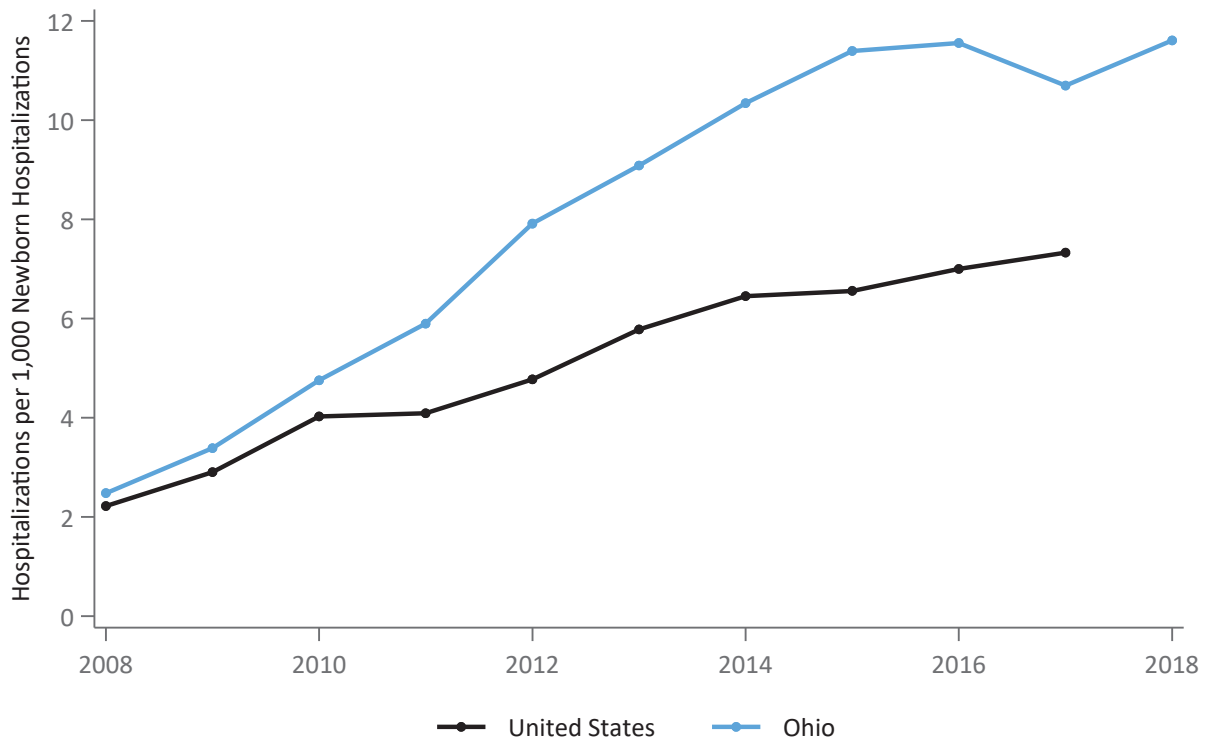
Note: Sample includes individuals who misused prescription pain relievers within the past year.
Source: NSDUH.

- **NAS**

203. Trends in NAS for Ohio and the U.S. are reported in Exhibit 56. Between 2008 and 2017 (the most recent year for which national data are available), NAS increased by 331 percent in Ohio compared to 230 percent for the U.S. While national data for 2018 are not available, NAS rates in Ohio increased in 2018. Overall, NAS increased by 368 percent in Ohio between 2008-18.

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Exhibit 56

NAS Hospitalization Rate
U.S. vs. Ohio

Note: 2008-2014 data are based on ICD-9 while 2016-2018 are based on ICD-10.
Source: HCUP.

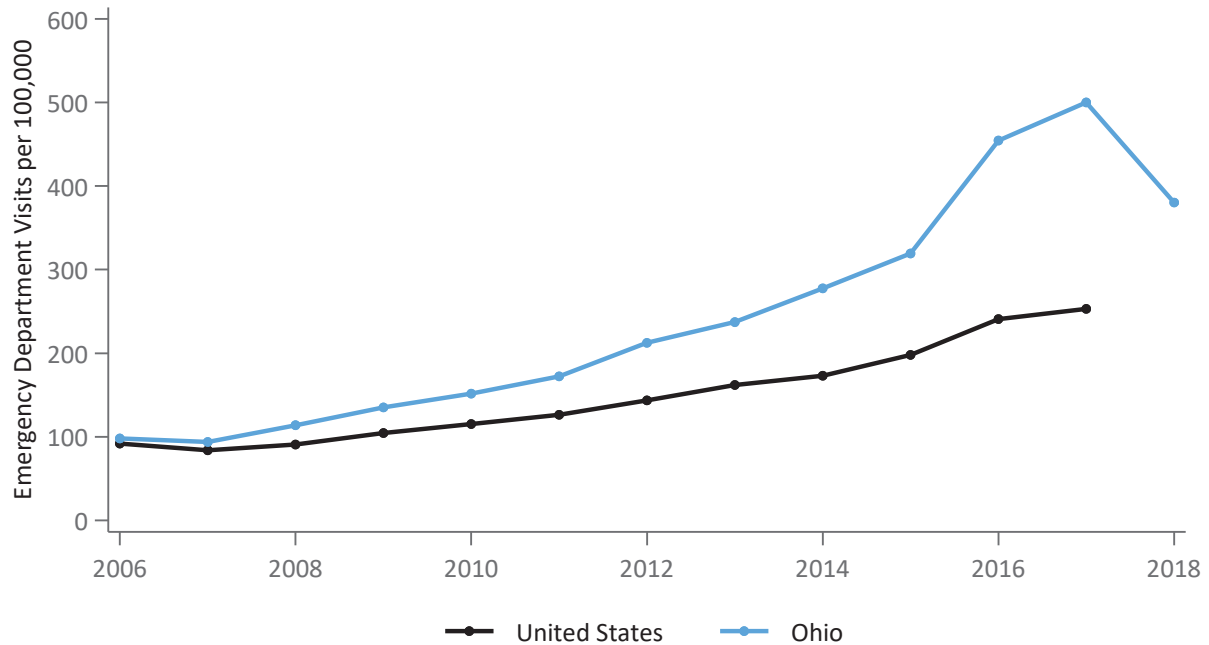
- *Opioid Related Emergency Department Visits and Hospitalizations*

204. Exhibit 57 reports the rate of opioid-related emergency department visits for Ohio and the U.S. between 2006 and 2017, the most recent year for which national data are available. Over this period, such visits increased by 411 percent in Ohio, substantially more than the 175 percent increase for the U.S. Exhibit 58 reports similar data for opioid-related inpatient hospital stays. Between 2006 and 2017, the peak year of inpatient stays in Ohio, such stays increased by 178 percent in Ohio, nearly double the 90 percent increase observed for the U.S.

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Exhibit 57

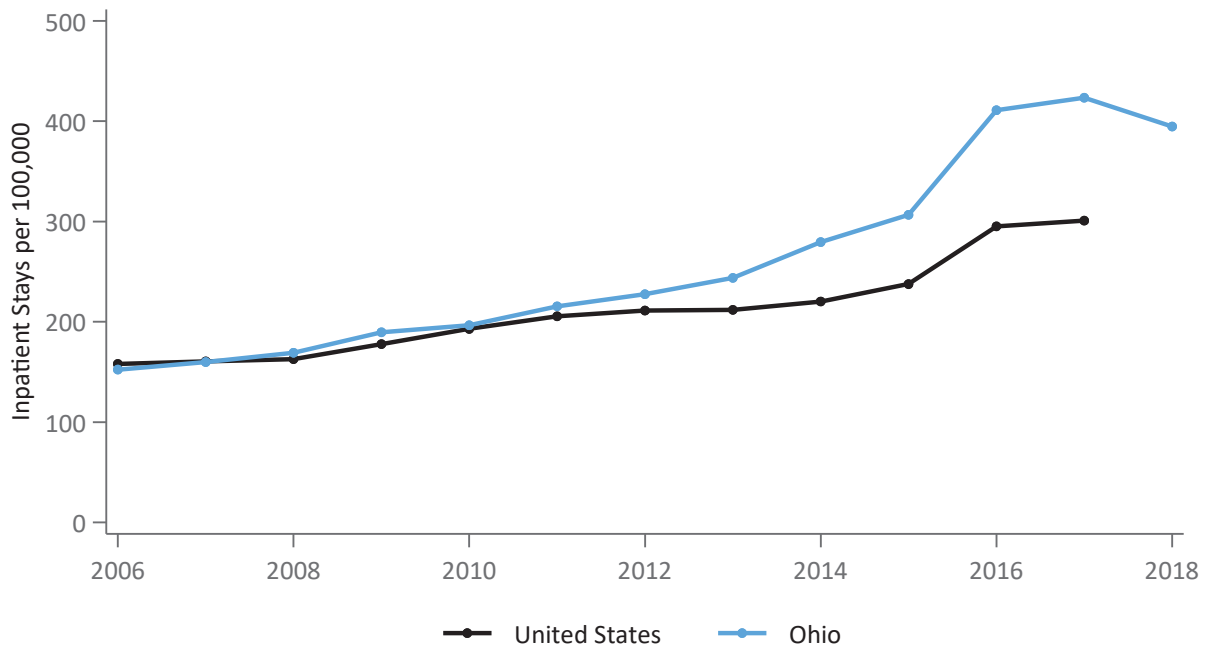
Opioid-Related Emergency Department Visit Rate U.S. vs. Ohio



Note: Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
Source: HCUP.

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Exhibit 58

Opioid-Related Inpatient Stay Rate
U.S. vs. Ohio

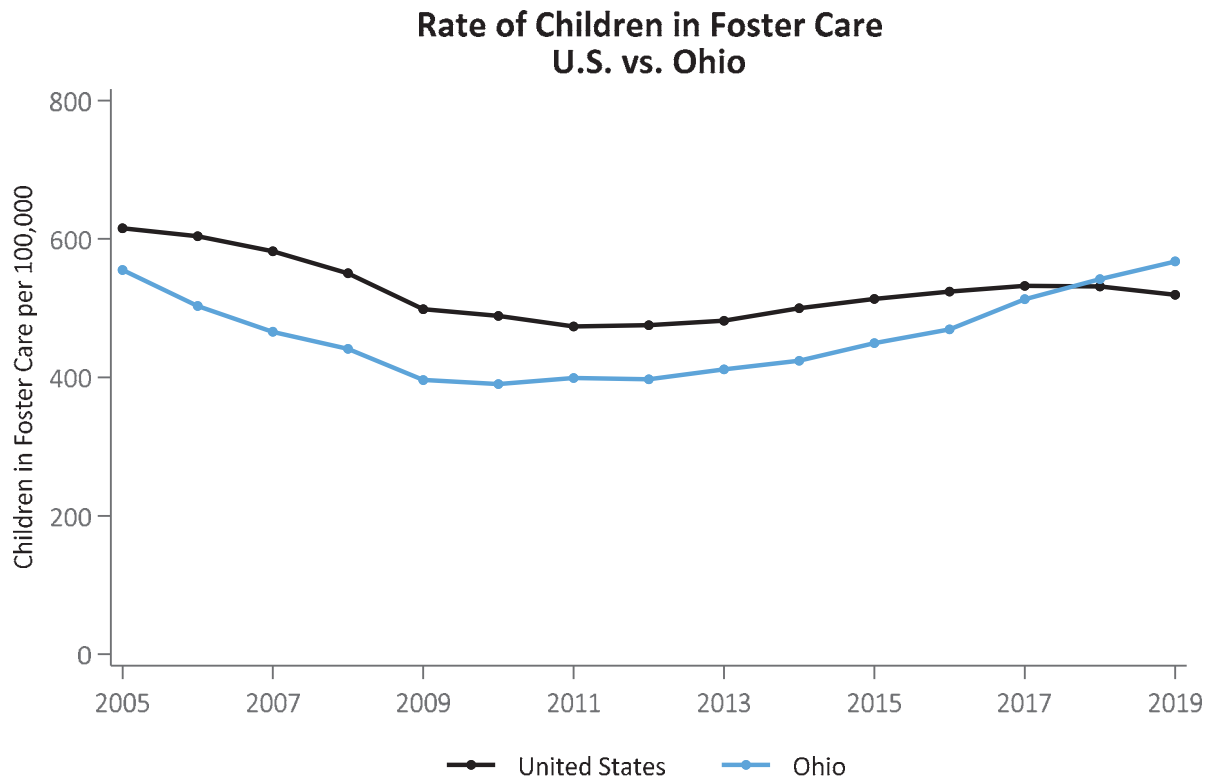
Note: Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
Source: HCUP.

- *Foster Care Placements*

205. As discussed in Section III above, state-level data on foster care placements are available for 2005-19 from the HHS's Adoption and Foster Care Analysis and Reporting System (AFCARS). Exhibit 59 shows that foster care placement rates gradually declined, both in Ohio and for the U.S., between 2005 and 2011. The Ohio rate was below the U.S. rate throughout this period. The downward trend in the foster case placement rate in Ohio reversed in 2009, increasing from 396 per 100,000 children in 2009 to 568 in 2019. Around the same time, the foster care placement rate for the U.S. stopped declining but did not increase as quickly as in Ohio. The Ohio rate exceeded the U.S. for the first time in 2018.

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Exhibit 59



Note: United States data is calculated as the national average foster care placement weighted by child population.
Source: AFCARS.

206. In sum, opioid-related harms other than mortality increased in Ohio as well as the United States over the period covered by available data. In each case, increases in these harms in Ohio are greater than those observed for the U.S., a pattern consistent with the higher level of shipments to Ohio and the dramatic increases in illicit opioid activity in the state after 2010.

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CONCLUSIONS TO CHAPTER 2

207. Trumbull and Lake counties, like other areas of Ohio, experienced dramatic growth in shipments of prescription opioids between the mid-1990s and 2010, and both also experienced large increases in prescription opioid mortality over that period. As the availability of prescription opioids became more limited, many users turned to illicit opioids. Trumbull and Lake counties provide an early example that users turn from prescription opioids to heroin when prescription opioids are not available and experienced increases in illicit opioid mortality, starting in the mid-2000s. When supplies for prescription opioids became more limited during Phase 2 of the crisis, Trumbull and Lake counties experienced large increases in illicit opioid mortality, a trend that accelerated as fentanyl become widespread in the area after 2013. In the process, Trumbull and Lake counties have experienced opioid mortality rates that are among the highest in the nation.

208. While comprehensive data on other opioid harms are not available for Trumbull and Lake counties, statewide data indicate that trends in OUD, HUD, NAS, foster care placements, and opioid-related emergency department visits and hospital stays grew more in Ohio than for the national as a whole.

209. My analysis, together with analysis by other experts, conservatively estimates that defendants' misconduct resulted in 240 deaths in Lake County and 241 deaths in Trumbull County between 1996 and 2019, and in turn the host of economic and social problems that result from excessive opioids. The number of deaths in these counties due to defendants' misconduct will unfortunately continue to grow in the future as preliminary national data for 2020 indicate that opioid mortality increased from 2019 levels.

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April 16, 2021

A handwritten signature in black ink, appearing to read "David M. Cutler". The signature is written in a cursive, flowing style.

David M. Cutler

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Appendix 1: Curriculum Vitae

David M. Cutler

Department of Economics
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Employment

2014-2019: Harvard College Professor, Harvard University

2005-: Otto Eckstein Professor of Applied Economics, Department of Economics and Kennedy School of Government, Harvard University

2003-2008: Social Sciences Dean, Faculty of Arts and Sciences, Harvard University

1997-2005: Professor of Economics, Department of Economics and Kennedy School of Government, Harvard University

1995-1997: John L. Loeb Associate Professor of Social Sciences, Harvard University

1993: On leave as Senior Staff Economist, Council of Economic Advisers and Director, National Economic Council

1991-1995: Assistant Professor of Economics, Harvard University

Other Affiliations

Academic and Policy Advisory Board, Kyruss, Incorporated

National Advisory Board, Firefly

Board Member, Center for Healthcare Transparency

Consultant, Mathematica Policy Research, Inc.

Consultant, Mercer Health & Benefits, LLC

Fellow, Employee Benefit Research Institute

Litigation. Retained by counsel for plaintiffs to provide expert services in pending litigation involving opioid pharmaceuticals.

Member, Institute for Research on Poverty

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Member, Institute of Medicine

Member, National Academy of Social Insurance

Research Associate, National Bureau of Economic Research, Aging, Health Care, Public Economics, and Productivity programs

Scientific Advisory Board, Alliance for Aging Research

Scientific Advisory Board, F-Prime Capital Partners (formerly Scientific Advisory Board, Fidelity Investments)

Senior Fellow, Center for American Progress

Public Service

2012-: Health Policy Commission, Commonwealth of Massachusetts

2006-2012: Group Insurance Commission, Commonwealth of Massachusetts

2002: Institute of Medicine Panel, "Vaccine Purchase Strategies in the United States"

2001: Institute of Medicine Panel, "Priority Areas for Quality Improvement"

2000: Medicare Technical Advisory Panel

1999: National Academy of Sciences Panel, New Horizons in Health: An Integrative Approach

1998: National Academy of Sciences Panel, Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health

1998-2002: National Institutes of Health Study Section Reviewer

1994-95: Technical Panel, Advisory Council on Social Security

1993: Senior Economist, Council of Economic Advisors, and Director, National Economic Council.

Honors and Awards

2018: Carpenter Award, Babson College

2014: Harvard College Professor, Harvard University

2011: MetLife Silver Scholar Award, Alliance for Aging Research

2011: Distinguished Leadership Award, Center for Connected Health, Partners Health Care

2009: John P. McGovern Award from the Association of Academic Health Centers

2007: Elected to American Academy of Arts and Sciences

2007: Named one of the 50 most influential men under age 45 by *Details* magazine

2006: Named one of "30 For The Future" by *Modern Healthcare* magazine, August 2006

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2006: Biennial award for distinguished contribution to the literature in population, Section on the Sociology of Population of the American Sociological Association, for "The Role of Public Health Improvements in Health Advances: The 20th Century United States"

2006: American Society of Health Economists Medal, Outstanding Health Economist Age 40 and Under

2004: David Kershaw Prize, Association for Public Policy and Management

2004: John Eisenberg Mentoring Award, Agency for Health Care Quality and Research

2003: Eugene Garfield Award, Research!America, for "The Return to Biomedical Research: Treatment and Behavioral Effects"

2001: Elected to Institute of Medicine

2000: Kenneth Arrow Award, Best Paper in Health Economics, for "How Does Managed Care Do It?"

2000-2001: Fellow, Center for Advanced Study in Behavioral Sciences

1999: Griliches Prize, best paper in *Quarterly Journal of Economics*, for "Are Medical Prices Declining?"

1999: Outstanding Mentor Award, Harvard University Graduate School of Arts and Sciences

1991: Honorable Mention, Outstanding Dissertation, National Academy of Social Insurance

1987: Phi Beta Kappa

Education

Ph.D. (Economics), M.I.T., September 1991.

A.B. (Economics, Summa Cum Laude) Harvard, 1987.

Professional Service

Former Member, Board of Directors, International Health Economics Association

Former Editor, *Journal of Health Economics*

Former Associate Editor, *Journal of Economic Perspectives*

Former Associate Editor, *Journal of Public Economics*

Former Associate Editor, *World Health Organization Bulletin*

Research Funding

Commonwealth Foundation

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Kaiser Family Foundation
Lasker Foundation
Pfizer
Pharmaceutical Research and Manufacturers Association
Robert Wood Johnson Foundation
Russell Sage Foundation
Rx Foundation
Alfred P. Sloan Foundation
U.S. Agency for Health Care Policy and Research
U.S. Department of Labor
U.S. National Institute of Health
U.S. Social Security Administration

Primary Fields

Health Economics
Public Economics

Books

Your Money or Your Life: Strong Medicine for America's Health Care System, Oxford University Press, 2004.

The Quality Cure: How Focusing on Health Care Quality Can Save Your Life and Lower Spending Too, University of California Press, 2014.

Edited Books

The Changing Hospital Industry: Comparing Not-for-Profit and For-Profit Hospitals, Chicago: University of Chicago Press, 1999.

Medical Care Output and Productivity, Chicago: University of Chicago Press, 2001 (with Ernst Berndt).

Frontiers in Health Policy Research, Volume 6, online as *Forum for Health Economics and Policy*, 2003 (with Alan Garber).

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Frontiers in Health Policy Research, Volume 8, online as *Forum for Health Economics and Policy*, 2005 (with Alan Garber).

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Frontiers in Health Policy Research, Volume 10, online as *Forum for Health Economics and Policy*, 2007 (with Alan Garber and Dana Goldman).

Health at Older Ages: The Causes and Consequences of Declining Disability Among the Elderly, University of Chicago Press, 2009 (with David Wise).

Measuring and Modeling Health Care Costs, Chicago: University of Chicago Press, 2018 (with Ana Aizcorbe, Colin Baker, and Ernst Berndt).

Articles

“Trends and Racial Differences in First Hospitalization for Stroke and 30-Day Mortality in the US Medicare Population From 1988 to 2013.” *Medical Care*. 2019;57(4):262-269 (with Jamie Yao, Kaushik Ghosh, Marcelo Coca Perrillon, and Margaret C. Fang)

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“Attribution of Health Care Costs to Diseases: Does the Method Matter?” in *Measuring and Modeling Health Care Costs*, 2018 (Ana Aizcorbe, Colin Baker, Ernst Berndt, and David Cutler, editors).

“The IT Transformation Health Care Needs” *Harvard Business Review*, 95(6), November 2017, 129-136 (with Nikhil Sahni, Robert Huckman, Anuraag Chigurupati).

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Appendix 2: Materials Relied Upon

Legal Documents

National Prescription Opiate Litigation, MDL No. 2804, Case No. 1:17-md-2804, Case Track Three Plaintiffs' Motion for Leave to File Amended Complaints, Exhibit B.

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Data Sources

AFCARS

ARCOS

CDC Wonder

Census Data

DEA, Diversion Control Division

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HCUP

NCHS Mortality Data

NSDUH Survey

Substance Abuse & Mental Health Data Archive's Public-use Data Analysis System (PDAS)

Substance Abuse & Mental Health Data Archive's Restricted-use Data Analysis System (RDAS)

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Appendix 3: Data Appendix

1. This appendix summarizes the major sources of data used in the analysis in this report and documents technical issues addressed in processing and analyzing these data. The first section addresses the CDC mortality data; the next addresses the ARCOS prescription shipments data; the next section addresses the non-mortality harms data; and the final section addresses the state- and county-level economic and demographic variables used in the analysis.

A. CDC Mortality Data

Mortality Data Sources

2. The National Center for Health Statistics (NCHS), part of the Centers for Disease Control, constructs Multiple Cause of Death (MCOB) data.¹⁶⁸ The data are individual-specific, providing information on the individual's cause of death, and are based on death certificates.

3. Public MCOB data are available in machine-readable format for the years 1968 through 2019. However, these data contain some key limitations with respect to the geographic detail provided:

- From 1989-2004, the data identify state of residence but only identify county of residence for counties with population over 100,000.¹⁶⁹
- From 2005-2019, the data omit all geographic details including state.¹⁷⁰

¹⁶⁸ <https://www.cdc.gov/nchs/nvss/deaths.htm>

¹⁶⁹ From 1989-1993, this restriction is based on population from the 1980 decennial census; from 1994-2002, the restriction is based on population from the 1990 decennial census; from 2003-2004, the restriction is based on population from the 2000 decennial census.

¹⁷⁰ For the years 1989 through 2018, data were accessed through the National Bureau of Economic Research's SAS-formatted datasets, available here: <https://www.nber.org/data/vital-statistics-mortality-data-multiple-cause-of-death.html>. For the year 2019, the NBER had not posted a formatted dataset at the time this report was prepared. As a result, raw data were accessed directly from the CDC, available at: https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm#Mortality_Multiple.

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4. To supplement the annual microdata files, I rely on aggregate data queried from CDC's Wide-ranging Online Data for Epidemiologic Research (CDC WONDER).¹⁷¹ This publicly available tool allows the user to query from the raw underlying MCODE data and can provide mortality counts at the state or county-level, provided that the total number of deaths covered by the query exceeds 10.

5. For county-level data, I construct a sample of 405 large counties for which there is a consistent time series with available mortality data covering the period 1993 through 2019. This generally corresponds to all counties with population of at least 100,000 based on the decennial census for the years 1980, 1990, and 2000. The counties included in the large county sample represent 70 percent of U.S. population as of 2010.

Cause of Death and Identifying Opioid-Related Overdose Mortality

6. The MCODE data include codes based on the World Health Organization's International Classification of Diseases (ICD) that can be used to identify whether a death was due to opioid overdoses.¹⁷² This is a system of codes frequently among practitioners to standardize diagnosis and treatment codes across data sources and geographies.¹⁷³ This system of codes is periodically revised. For the years 1999 through 2019, the MCODE mortality data incorporate the codes as defined by the 10th revision of ICD (known as ICD-10). From 1979 through 1998, the NCHS mortality data incorporate the 9th revision of ICD (known as

¹⁷¹ <https://wonder.cdc.gov/mcd.html>.

¹⁷² <https://web.archive.org/web/20190324051703/http://www.who.int/health-topics/international-classification-of-diseases>.

¹⁷³ In addition to use in classification of causes of death in mortality data, the ICD system is also used in coding and classifying diagnosis and morbidity data at inpatient and outpatient medical facilities through the ICD-10 CM (clinical modification) system. <https://www.cdc.gov/nchs/icd/index.htm>. For background on the development and accuracy of the ICD code system, see: O'Malley, Kimberly J., Karon F. Cook, Matt D. Price, Kimberly Raiford Wildes, John F. Hurdle, and Carol M. Ashton, "Measuring diagnoses: ICD code accuracy" Health services research vol. 40,5 Pt 2 (2005): 1620-39.

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ICD-9). As discussed in more detail below, I account for revisions to the code systems as necessary.

7. Each record in the MCODE mortality data contains two forms of ICD codes:

- A single code for the “Underlying Cause of Death”
- Up to 20 additional codes for the “Multiple Causes of Death”

8. Based on these two sets of codes, I identify all deaths in a given year in which opioids are identified as a cause of death. In doing so, I follow the procedures developed by the CDC to identify and classify drug overdoses as opioid-related:

- The CDC’s “Annual Surveillance Report of Drug-Related Risks and Outcomes” for the year 2019 identifies opioid-related codes used by the CDC under ICD-10.¹⁷⁴
- “The Numbers Behind the Opioid Crisis,” a 2017 report prepared by the Social Capital Project for the Joint Economic Committee of Congress, outlines opioid-related codes used by the CDC under ICD-9.¹⁷⁵

9. For ICD-10, I further categorize opioid-related drug overdoses based on the type of opioid involved:

- Prescription Opioids
- Heroin
- Fentanyl

10. The codes used in the analysis are identified in Appendix Exhibit 3.1.

¹⁷⁴ <https://www.cdc.gov/drugoverdose/pdf/pubs/2019-cdc-drug-surveillance-report.pdf>

¹⁷⁵ https://www.jec.senate.gov/public/_cache/files/d0c91be3-1d94-4c58-9ffb-32ffc8543631/3-17-numbers-behind-opioid-crisis.pdf

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Appendix Exhibit 3.1

ICD-9 and ICD-10 Codes Used to Identify Opioid-Related Overdose Mortality

Category	ICD-10 (1999-2018)		ICD-9 (1983-1998)	
	Underlying Cause	Contributing Cause	External Cause of Injury	Diagnosis
Any Opioid Mortality	X40 X41 X42 X43 X44 X60 X61 X62 X63 X64 X85 Y10 Y11 Y12 Y13 Y14	T40.0 T40.1 T40.2 T40.3 T40.4 T40.6	E850 E851 E852 E853 E854 E855 E856 E857 E858 E950.0 E950.1 E950.2 E950.3 E950.4 E950.5 E962.0 E980.0 E980.1 E980.2 E980.3 E980.4 E980.5	965.00 965.01 965.02 965.09
Detailed Opioid Type:				
Heroin	X40 X41 X42 X43	T40.1	N/A	
Prescription Opioids	X44 X60 X61 X62	T40.2		
Methadone	X63 X64 X85 Y10	T40.3		
Fentanyl	Y11 Y12 Y13 Y14	T40.4		
Other and Unidentified Opioid		T40.6		
Unidentified Drugs	X40 X41 X42 X43 X44 X60 X61 X62 X63 X64 X85 Y10 Y11 Y12 Y13 Y14	T50.9	E850 E851 E852 E853 E854 E855 E856 E857 E858 E950.0 E950.1 E950.2 E950.3 E950.4 E950.5 E962.0 E980.0 E980.1 E980.2 E980.3 E980.4 E980.5	965.9 977.9

Allocating Drug Overdoses with Unspecified Drug Types

11. There is a sizeable share of overdose deaths where the drug(s) contributing to the death are not identified in the MCOD data. For these deaths, I adapt a methodology initially developed by Christopher Ruhm in a series of papers in 2017 and 2018 to probabilistically allocate these unspecified drug overdoses to opioids and other causes based on the additional characteristics of decedents reported in the underlying data.¹⁷⁶

¹⁷⁶ Ruhm, Christopher J., "Geographic Variation in Opioid and Heroin Involved Drug Poisoning Mortality Rates." *American Journal of Preventive Medicine* 53, No. 6 (2017): 745-753; Ruhm, Christopher J., "Corrected US opioid-involved drug poisoning deaths and mortality rates, 1999–2015," *Addiction* 113 (2018): 1339-1344; Ruhm (2018).

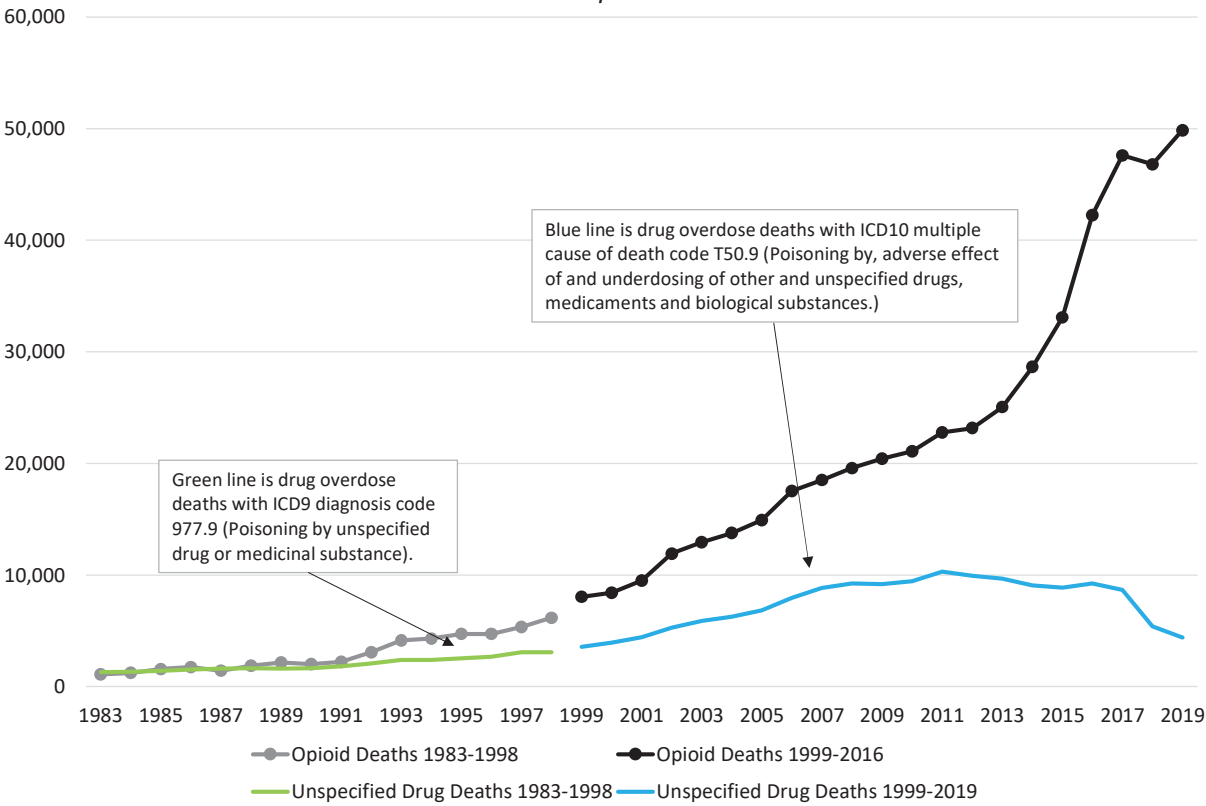
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12. This approach uses a probit regression to evaluate the relationship between demographic factors and whether a death was opioid-related based on individuals for whom the source of an overdose death was reported. Probit regressions were run on a year-specific basis for the years 1983-2019. Based on these results, it is possible to estimate the probability that an overdose death with unidentified causes was, in fact, opioid related. The results of this analysis are then use to construct national, state, and county-level time series of opioid overdose deaths. The county and state time series are limited due to the reporting restrictions in the public microdata (as described above) and thus this method is used to construct county and state datasets through 2004. For the years 2005 through 2019, county and state unclassified overdose deaths are allocated based on the ratios of opioid-related deaths to unclassified deaths from the national probit regressions.

13. Appendix Exhibit 3.2 below plots overdose deaths where the cause was identified as opioid-related as well as overdose deaths where the drug involved was not specified. Appendix Exhibit 3.3 plots the results of the adjustment to allocate the unspecified drug deaths.

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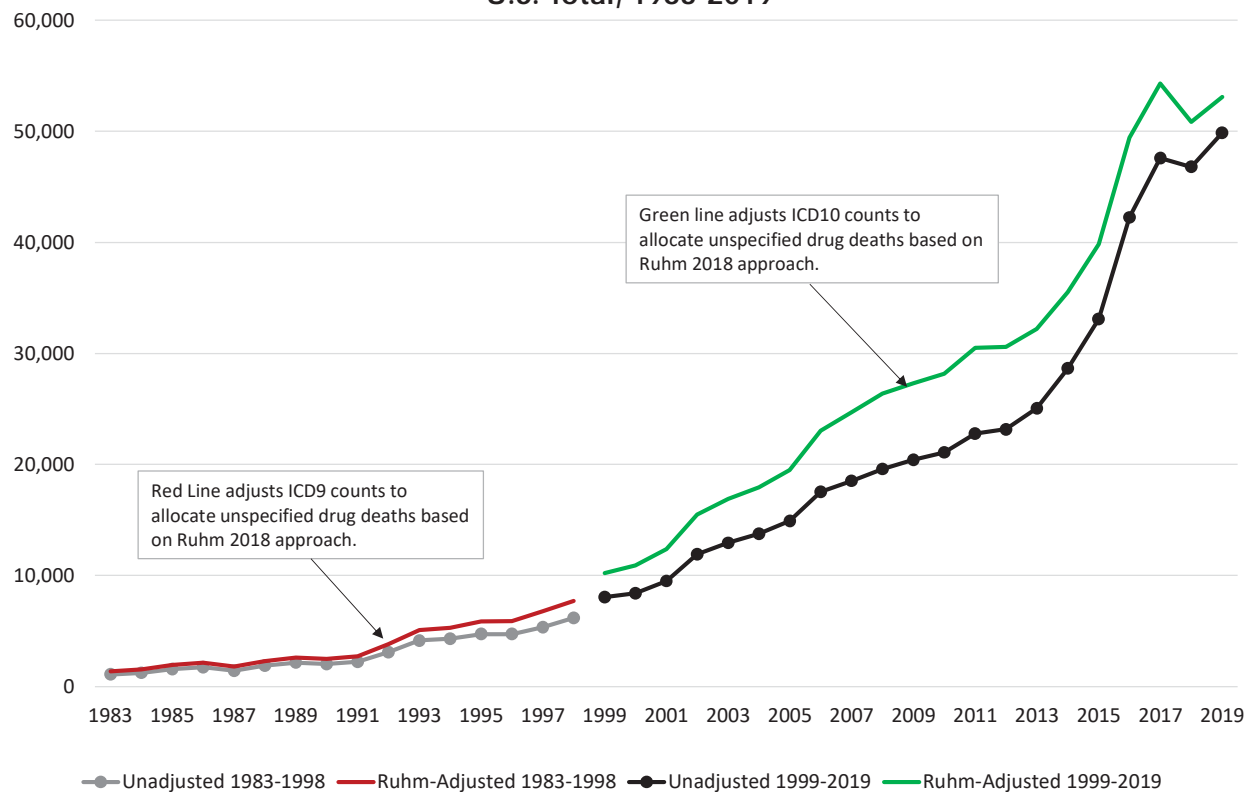
Appendix Exhibit 3.2
Opioid vs. Unspecified Overdose Deaths
U.S. Total, 1983-2019



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Appendix Exhibit 3.3

Impact of Adjustment for Unspecified Drug Overdoses on Opioid Deaths U.S. Total, 1983-2019



14. There is also a sizeable share of drug overdoses identified as opioid-related but for which the data do not specify whether they are due to prescription opioids, heroin or other substances. I follow the general procedures outlined in Ruhm (2018) to further allocate opioid overdoses where the type of opioid involved is not reported in the MCOD data into detailed categories:

- Prescription opioids
- Illicit opioids (including heroin and fentanyl)
- Illicit opioids by type

15. This approach also uses a probit regression to evaluate the relationship between demographic factors and the type of opioid, based on mortalities for which the detailed opioid

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type involved was reported. Regressions were run on a year-specific basis for the years 1999-2018. Based on these results it is possible to estimate the probability that an opioid-related death that does not identify the type of opioid involved was, in fact, attributable to the opioid categories identified above. After performing these regressions, national, state, and county-level time series for mortality rates for each of the three detailed opioid categories were constructed. As above, state and county time series were constructed based on the regression results through 2004. From 2005-2018, state and county allocations were constructed based on the national ratios as determined by the regression results for those years.

Adjusting for the ICD9 to ICD10 transition

16. As noted above, the ICD code system is periodically updated. The CDC warns that when comparing mortality rates across regimes, differences in the coding regimes can distort the analysis of time series trends.¹⁷⁷

17. In order to account for the transition from ICD-9 to ICD-10, the ICD-9 mortality rates are adjusted by the Comparability Ratio calculated in Hoyert et al. (2001).¹⁷⁸ This ratio was based on the review of a sample of death records which were categorized separately under both ICD9 and ICD 10. Based on this sample, the authors developed a comparability ratio for “Drug-Induced Deaths” of 1.195, indicating that mortality rates under ICD-9 should be adjusted upward by about 20 percent in order to be comparable to rates under ICD-10.¹⁷⁹

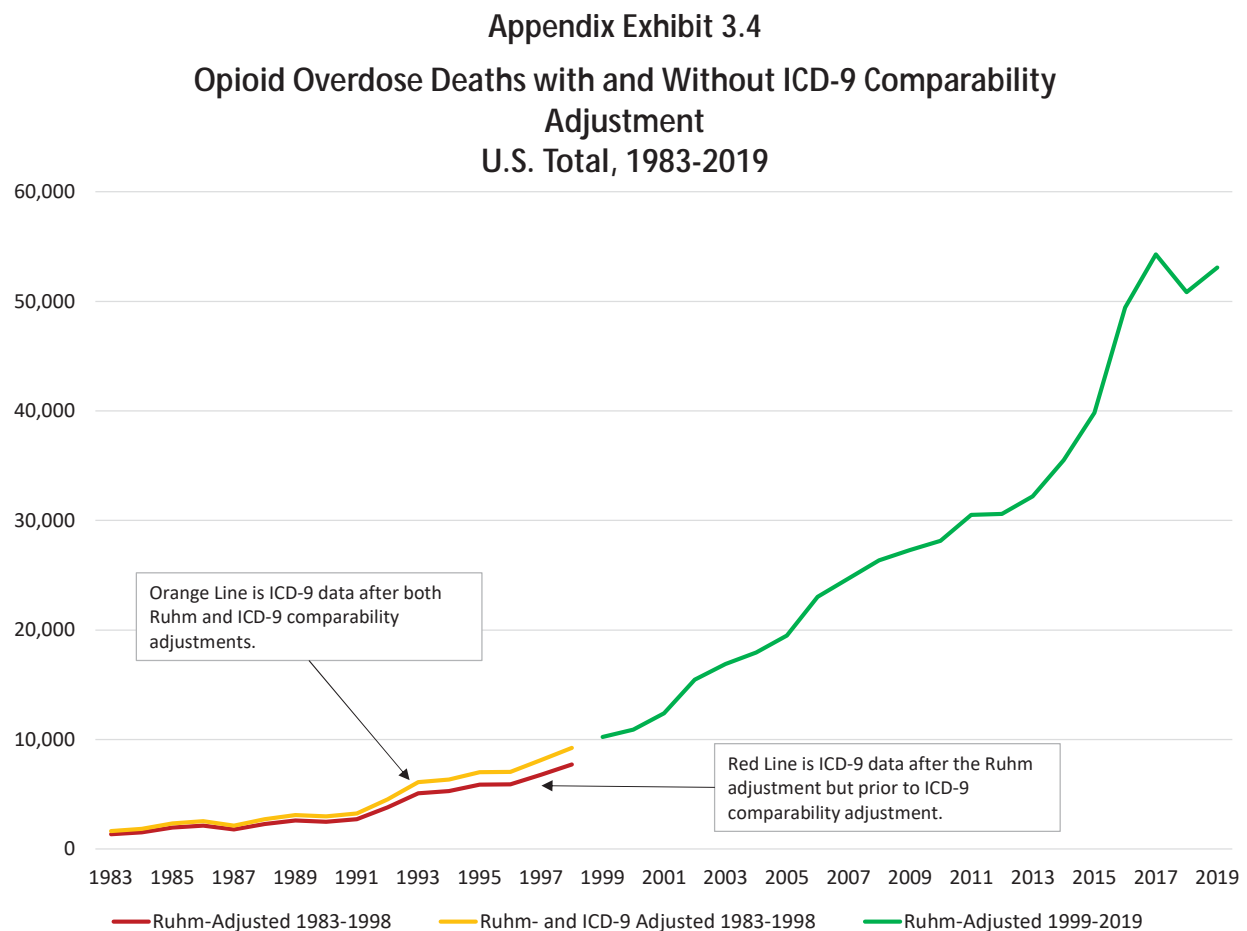
¹⁷⁷ Anderson, Robert N., Aialdi M. Minino, Donna L. Hoyert, and Harry M. Rosenberg, “Comparability of Cause of Death Between ICD-9 and ICD-10: Preliminary Estimates,” *National Vital Statistics Report* 49, No. 2 (2001): 1-32.

¹⁷⁸ Hoyert, Donna L., Elizabeth Arias, Betty L. Smith, Sherry L. Murphy, Kenneth D. Kochanek, “Deaths: Final Data for 1999,” *National Vital Statistics Reports* 49 No. 8 (2001): 1-114.

¹⁷⁹ Note that the category “Drug-Induced Deaths” is broader than deaths due to drug overdoses.

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18. The impact of the adjustment of ICD-9 data is shown in Appendix Exhibit 3.4, which demonstrates continuity between the adjusted data from the ICD-9 regime and the ICD-10 regime.



B. ARCOS Prescription Shipment Data

19. The Drug Enforcement Agency (DEA) provides data on shipments of prescription opioids over time and across geographies. This appendix describes the source of these data and the steps taken to process and set up the data for analysis.

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DEA ARCOS Data

20. The Controlled Substances Act of 1970 requires all manufacturers and distributors of controlled substances to report the details of their shipments of controlled substances to the federal government. The DEA is responsible for managing and organizing this reporting process and sharing the data with investigative and regulatory agencies to monitor diversion of controlled substances to illicit markets.¹⁸⁰

21. The DEA has developed a data collection and reporting system known as the Automation of Reports and Consolidated Orders System (“ARCOS”). The DEA releases publicly available annual reports summarizing the ARCOS data.¹⁸¹ These public reports, known as Retail Drug Summary Reports, identify the total grams of each controlled substance shipped to retail registrants. Table 1 in these public reports summarizes shipments at the most detailed level available: by 3-digit zip code, by DEA drug code, and by quarter-year.

22. My analysis focuses on the following opioid drug codes in the ARCOS data¹⁸²:

Appendix Exhibit 3.5
DEA ARCOS Opioid Drug Codes and Names

DEA Drug Code	Drug Name
9050	CODEINE
9143	OXYCODONE
9150	HYDROMORPHONE
9193	HYDROCODONE
9230	MEPERIDINE (PETHIDINE)
9300	MORPHINE
9652	OXYMORPHONE
9780	TAPENTADOL
9801	FENTANYL BASE

¹⁸⁰ <https://www.deadiversion.usdoj.gov/arcos/index.html>

¹⁸¹ https://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html

¹⁸² The data also include non-opioid controlled substances such as Amphetamine and additional opioid products with small or incomplete data (such as Opioid Powder and Dihydrocodeine).

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23. DEA drug codes identify the molecule of the controlled substance, but not the dosage size, brand name, or format of the substance (i.e., tablet, transdermal patch, or solution). For example, shipments of OxyContin would be classified under the drug code 9143 Oxycodone along with all other branded and generic opioids containing Oxycodone. In analyzing the ARCOS data, I focus on opioids typically used for treatment of pain and not for medically assisted treatment of use disorder. I thus exclude shipments of Buprenorphine (Drug Code 9064) and Methadone (Drug Code 9250B).¹⁸³

24. The DEA website includes public reports in PDF format covering the years 2000-2019. Data from Table 1 of these reports were processed and converted into machine readable format. Additional reports covering the years 1997, 1998, and 1999 were identified based on an archived version of the DEA website available through the Internet Archive.¹⁸⁴ These data were processed in the same way.

DEA Schedule

25. Under the Controlled Substances Act, the DEA classifies drugs into five categories based on their medical purpose and the potential for abuse or dependency. Schedule I includes heroin and other illegal narcotics that are not accepted for medical use. Schedule II drugs are accepted for medical use but have “high potential for abuse, with use leading to severe psychological or physical dependence.”¹⁸⁵ Schedule III drugs are also accepted for medical use

¹⁸³ While there are forms of Buprenorphine and Methadone that are prescribed for the treatment of pain, most shipments of these drugs are for use in treatment of use disorder. The ARCOS public reports do not permit disaggregation by use case; however, the data do report total national shipments in grams by “business activity” including pharmacies and narcotic treatment programs which dispense Methadone for treatment of use disorder. In 2010, there were a total of 8.7 million grams of Methadone shipped to such narcotic treatment programs, 44% more than total grams of Methadone shipped to pharmacies.

¹⁸⁴ https://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/2010/2010_rpt7.pdf.
¹⁸⁴ https://web.archive.org/web/20090320043126/https://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html

¹⁸⁵ <https://www.dea.gov/drug-scheduling>.

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and have moderate to low potential for abuse or dependence. Most prescription opioids, including oxycodone, are classified by the DEA as Schedule II. However, products containing fewer than 90 milligrams of codeine (typically in combination with acetaminophen) are classified as Schedule III. It is not possible to distinguish between shipments with the same underlying ingredients but different drug schedules in the public ARCOS datasets.

Morphine Milligram Equivalents (MMEs)

26. In order to compare shipments of different types of opioids, it is necessary to account for differences in the strength of the underlying opioid molecule. Consistent with the standard practice in the literature analyzing prescription opioids, I convert grams of the underlying substance into Morphine Milligram Equivalents (MMEs). For example, the CDC's prescribing guidelines for prescription opioids are expressed in MMEs.¹⁸⁶ Economic literature analyzing the links between prescription shipments and harms also typically convert ARCOS shipments to MMEs.¹⁸⁷

27. In order to convert the ARCOS shipments data to MMEs, I rely on conversion factors commonly used in the literature.¹⁸⁸ By multiplying shipments in grams by the conversion factor and dividing by 1,000, shipments can be expressed in MMEs. The conversion factors applied are summarized in Appendix Exhibit 3.6.

¹⁸⁶ <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>

¹⁸⁷ See: Alpert, Abby, David Powell, and Rosalie Liccardo Pacula, "Supply-Side Drug Policy In The Presence of Substitutes: Evidence From The Introduction Of Abuse-Deterrent Opioids," American Economic Journal: Economic Policy, 2018, 10(4): 1-35; Ruhm (2018).

¹⁸⁸ <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf>

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Appendix Exhibit 3.6
MME Conversion Factors

DEA Drug Code	Drug Name	MME Conversion Factor
9050	CODEINE	0.15
9143	OXYCODONE	1.50
9150	HYDROMORPHONE	4.00
9193	HYDROCODONE	1.00
9230	MEPERIDINE (PETHIDINE)	0.10
9300	MORPHINE	1.00
9652	OXYMORPHONE	3.00
9780	TAPENTADOL	0.40
9801	FENTANYL BASE ¹⁸⁹	100.00

Allocating Shipments from 3-Digit Zip Codes to Counties

28. As noted above, the most detailed geographic area reported in the public ARCOS reports is the 3-digit zip code. 3-digit zip codes are based on the first three digits of standard US postal zip codes. These areas typically (but not exclusively) span across more than one county and thus are not directly comparable to the county-level data available for mortality, crime, and demographic and economic statistics.

29. In order to link the ARCOS shipments data to the other county data, I have allocated shipments based on the weighted average population of census block centroids (center points) that fall within each county that a 3-digit zip code crosses. This means that when a 3-digit zip code crosses county boundaries, the population at the census block level is used to estimate the share of population across counties for the 3-digit zip. An assumption underlying this approach is that the shipments per capita within a 3-digit zip code are the same

¹⁸⁹ MME factors for Fentanyl used by medical practitioners depend in part on the transmittal mechanism, as prescription Fentanyl is typically contained in transdermal patches or lozenges. The DEA ARCOS data aggregates shipments of Fentanyl across types into total grams of the base drug. In order to convert these total grams of Fentanyl to MMEs, a factor of 100 is applied, consistent with the literature which applies the same factor to convert parenteral Fentanyl to morphine equivalents. See, footnote 8 from: <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf>

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across census blocks. This is a standard method used to perform this type of geographic allocation.¹⁹⁰

30. Census block centroids are useful as a translation unit because both 3-digit zip codes and counties are large compared to census blocks and county borders perfectly match census geographies. Additionally, since drug shipments are sold to end-users, population weighting is preferable to area weighting.

31. To do this, the census blocks fall within each 3-digit zip are first identified. Then I determine which counties each of those blocks belong to and compute the share of the 3-digit zip's population that falls within that county, based on 2010 population from the US Census. Finally, the ARCOS drug shipment totals are attributed to those counties according to their population share.

$$Qc_i = \sum_{j=1}^n Qz_j \frac{Pc_{ij}}{Pz_j}$$

Given:

Qc_i = Quantity in county i
 Qz_j = Quantity in zip j
 Pc_{ij} = Population in county i and zip j
 Pz_j = Population in zip j

32. After this allocation, the dataset with county-level shipments by drug code and quarter-year can be combined with other county-level information used in the analysis.

¹⁹⁰ For example, Rolheiser et al. (2018) perform a similar allocation to convert county-level prescribing rates to Congressional districts based on census block population weights. Rolheiser, Lyndsey A., Jack Cordes, BSPH, S.V. Subramanian, "Opioid Prescribing Rates by Congressional Districts, United States, 2016," American Journal of Public Health, 108, no. 9 (September 1, 2018): pp. 1214-1219.

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Interpolation for Year 2000

33. The DEA public report for calendar year 2000 contains shipments for only a subset of the drug codes used in the other years. While oxycodone and hydrocodone are reported, remaining opioids including morphine are not. In order to account for this change in reporting and to create a consistent time series, I have interpolated shipments for the omitted drug codes at the county level. For each county and omitted drug code, I interpolate shipments in the year 2000 as the midpoint between shipments in the years 1999 and 2001.¹⁹¹

Shipments per Capita per Day

34. In order to account for differences in population across counties, total MMEs are converted into MMEs per adult by dividing by US Census data reporting adult population (aged 15 plus) for each county and year in the data. Finally, in order to express the units in easier-to-interpret scales, shipments are expressed as MMEs per capita per day by dividing the per adult shipments by 365. This is the unit of shipments used throughout the analysis and is interpreted as the volume of MMEs shipped to retail registrants in a county per adult and per day in a given year. I refer to this as “shipments per capita per day.”

C. Non-Mortality Harm Metrics

35. This section describes the sources used for opioid-related harms other than mortality.

¹⁹¹ According to national opioid shipment data provided by the International Narcotics Control Board, shipments in MMEs per capita in the US in the year 2000 were close to the mid-point between 1999 and 2001. The midpoint of 1999 and 2001 from these data (excluding Methadone) is 171.98, compared to actual value of 171.82. http://web.archive.org/web/20151009170340/http://www.painpolicy.wisc.edu/sites/www.painpolicy.wisc.edu/files/country_files/morphine_equivalence/unitedstatesofamerica_me.pdf

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- **Opioid-Related Emergency Department Visits and Inpatient Stays**

36. The Healthcare Cost and Utilization Project (HCUP) is a family of datasets published by the Agency for Healthcare Research and Quality (AHRQ) that collect information on hospital and emergency room care in partnership between federal and state governments and the health care industry.¹⁹² HCUP provides a “Fast Stats” portal that summarizes data on opioid-related hospital care at the state and national levels.¹⁹³ Because the HCUP data switch from reporting based on the ICD-9 system to the ICD-10 system Q4 of 2015, annual rates are calculated for years ending in the 3rd quarter of each year (e.g., 2015 represents the period spanning from Q4 2014 through Q3 2015). State participation in HCUP is voluntary and not all states participate in all periods.

- **Rate of Children in Foster Care**

37. The U.S. Department of Health and Human Services (HHS) collects and reports information on children in foster care through the Adoption and Foster Care Analysis and Reporting System (AFCARS).¹⁹⁴ AFCARS provides state-level data on the number of children in foster care from 2005 through 2018. For 1995 through 2004, national data provided by the U.S. House Ways and Means Committee Green Book are used.¹⁹⁵ The data report the number of children in foster care relative to the total number of children in the state, multiplied by

¹⁹² <https://www.hcup-us.ahrq.gov/>.

¹⁹³ <https://www.hcup-us.ahrq.gov/faststats/OpioidUseMap>.

¹⁹⁴ <https://www.acf.hhs.gov/cb/data-research/adoption-fostercare>.

¹⁹⁵ <https://greenbook-waysandmeans.house.gov/sites/greenbook.waysandmeans.house.gov/files/Figure%2011-3%20and%20Table%2011-3.pdf>.

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100,000. In order to be comparable to the AFCARS data, the Green Book rates are adjusted based on the ratio where the two sources overlap (the period from 2005 through 2016).

- **Neonatal Abstinence Syndrome (NAS) Rate**

38. HCUP provides a Fast Stats portal that reports annual data on NAS rates for the nation and by state.¹⁹⁶ The data report NAS rates as the number of newborn hospitalizations due to NAS relative to the total number of newborn hospitalizations, multiplied by 1,000. As with the HCUP data on emergency department visits and inpatient stays, the code system used by HCUP transitioned from ICD-9 to ICD-10 in 2015. Data from 2016 through 2018 are based on the ICD-10 reporting system.

- **Drug Confiscations by Type from NFLIS**

39. The DEA's National Forensic Laboratory Information System (NFLIS) provides data on from forensic analysis of substances submitted to state and federal laboratories as part of criminal drug cases.¹⁹⁷ The DEA provides annual data identifying the number of submitted cases by detailed drug type and by state for the years 2007 through 2019.

D. State and County Level Demographic and Economic Variables

40. This section describes the sources used for construction of state and county level demographic and economic variables and, if applicable, the method of interpolation used to estimate data for any missing years. Appendix Exhibit 3.7 below reports the data sources and years for which the data are available by variable category.

¹⁹⁶ <https://www.hcup-us.ahrq.gov/faststats/NASMap>.

¹⁹⁷ <https://www.nflis.deaiversion.usdoj.gov/NFLISHome.aspx>.

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Population Characteristics

41. Data on annual population and population characteristics by county were downloaded from the Census Bureau's Population Estimates Program (PEP).¹⁹⁸ These data are available on an annual basis from 1990 to 2019.

Education

42. Data on the distribution of educational attainment by county and state from 1990 to 2018 were created from two sources: (1) decennial Census data from 1990 and 2000; and (2) the 5-year American Community Survey (ACS) as compiled by the National Historical Geographic Information System (NHGIS).¹⁹⁹ To create an annual time series, data are interpolated for years not reported in either the Decennial Census or the 5-year ACS data. Data from the decennial census are used for 1990 and 2000. Where ACS 5-year estimates are available, the midpoint of each 5-year period is used as an estimate of the value of the variable for that mid-point year (e.g. 2005-2009 is used for 2007, 2006-2010 is used for 2008, etc.) Linear interpolation is used to fill in gaps between available data points. Following linear interpolation, the 2017 data point is carried through to 2019. Based on these sources, the following education categories are constructed: less than high school; high school graduate (but not college); at least some college; college graduate or greater.

Median Household Income

43. Median household income data is obtained from the same sources and constructed in the same manner as the education statistics. Median household income is

¹⁹⁸ U.S. Census Bureau; Population Estimates Program: <https://www.census.gov/programs-surveys/popest.html>

¹⁹⁹ Manson, Steven, Jonathan Schroeder, David Van Riper, and Steven Ruggles. *IPUMS National Historical Geographic Information System: Version 13.0* [Database]. Minneapolis: University of Minnesota.

2018. <http://doi.org/10.18128/D050.V13.0>

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converted into 2010 dollars using annual BLS CPI data.²⁰⁰ When used in regression analyses, median household income is expressed in thousands of dollars.

Urban Percentage of the Population

44. This variable is defined as the number of people living in urban areas (including both urbanized areas and urban clusters) divided by the total number of people living in urban and rural areas. Urbanized areas and urban clusters are determined by the Census Bureau based on the population within a geographical area. This metric is available in the decennial Census data. Data in non-reporting years between 1990 and 2010 are estimated using linear interpolation between the available decennial census years. Data post-2010 is held constant and set at the 2010 level.

Poverty Status

45. Percentage of people living in poverty, by year, from 1990 to 2019 is constructed in a similar manner to the education and median household income time series. This variable is defined as the number of persons with income below poverty level divided by the total number of persons for whom poverty status is determined. The decennial census identifies people as below the poverty level based on their prior year income. The 5-year ACS surveys identify people whose past 12-month income was below poverty level (surveys are run continuously over the 5-year period).

Employment Statistics

46. Data on the labor force were obtained from the BLS's Local Area Unemployment Statistics program.²⁰¹ Data are available annually at the county level from 1990 to 2019. The unemployment rate is calculated from the BLS data as the number of unemployed persons

²⁰⁰ Bureau of Labor Statistics, CPI-All Urban Consumers (Current Series):

https://data.bls.gov/timeseries/CUUR0000SA0?output_view=pct_1mth

²⁰¹ Bureau of Labor Statistics; Local Area Unemployment Statistics: <https://www.bls.gov/lau/>

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divided by the total labor force. The employment to population ratio is calculated using the BLS's total number of employed persons divided by the Census total adult population age 15+. The employment to population ratio for males aged 25-54 (state only) was computed from BLS Current Population Survey (CPS) microdata made available through IPUMS.²⁰² CPS microdata are available on a monthly basis from 1990 to 2019. The CPS includes state, age, sex, and employment status information as well as a survey weight for each observation. For each state and month, a ratio is calculated using the weighted population of employed males aged 25-54 to the total civilian population of males aged 25-54. The monthly ratios are averaged by state and year to create an annual ratio.

Industry Characteristics

47. Data on industry characteristics were obtained from the US Census County Business Patterns data.²⁰³ Industry shares are calculated for each state or county as the number of employees in an industry divided by the number of employees in all classified industries (as identified by NAICS code). Data are available annually at the county level from 1990 to 2018.²⁰⁴ 2019 values are held constant at the 2018 level.

²⁰² Flood, Sarah, Miriam King, Renae Rodgers, Steven Ruggles and J. Robert Warren. Integrated Public Use Microdata Series, Current Population Survey: Version 7.0. Minneapolis, MN: IPUMS, 2020. <https://doi.org/10.18128/D030.V7.0>.

²⁰³ US Census Bureau; County Business Patterns: <https://www.census.gov/programs-surveys/cbp.html>

²⁰⁴ Pre-1990 data are also available and are used for calculation of the 10-year change in manufacturing employment. Prior to 1986, SIC codes were used by County Business Patterns. An SIC to NAICS code lookup (https://www.census.gov/eos/www/naics/concordances/1987_SIC_to_2002_NAICS.xls) was used to identify relevant manufacturing industry codes.

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Appendix Exhibit 3.7

Economic and Demographic Variables with Data Sources and Years Reported

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	
Population Characteristics																															
- Population																															
- Percent Male/Female	1990 PEP	1991 PEP	1992 PEP	1993 PEP	1994 PEP	1995 PEP	1996 PEP	1997 PEP	1998 PEP	1999 PEP	2000 PEP	2001 PEP	2002 PEP	2003 PEP	2004 PEP	2005 PEP	2006 PEP	2007 PEP	2008 PEP	2009 PEP	2010 PEP	2011 PEP	2012 PEP	2013 PEP	2014 PEP	2015 PEP	2016 PEP	2017 PEP	2018 PEP	2019 PEP	
- Percent <15, 15-29, 30-44, 45-64, 65+																															
- Percent White/Black/Other																															
- Percent Hispanic																															
Education																															
- Percent Less than High School	1990 Census										2000 Census																				
- Percent High School Only																															
- Percent Some College																															
- Percent College or Higher																															
Employment Statistics																															
- Employment to Population Ratio	1990 BLS	1991 BLS	1992 BLS	1993 BLS	1994 BLS	1995 BLS	1996 BLS	1997 BLS	1998 BLS	1999 BLS	2000 BLS	2001 BLS	2002 BLS	2003 BLS	2004 BLS	2005 BLS	2006 BLS	2007 BLS	2008 BLS	2009 BLS	2010 BLS	2011 BLS	2012 BLS	2013 BLS	2014 BLS	2015 BLS	2016 BLS	2017 BLS	2018 BLS	2019 BLS	
- Unemployment Rate																															
- Prime Age Male (25-54) Employment																															
- to Population Ratio (State Only)																															
Median Household Income																															
(Converted to 2010 Dollars using Annual CPI data)	1990 Census										2000 Census																				
Poverty Rate	1990 Census										2000 Census																				
Percent Urban	1990 Census										2000 Census																				
Industry Characteristics																															
- Percent Agriculture/Mining/Construction/Utilities																															
- Percent Manufacturing	1990 CBP	1991 CBP	1992 CBP	1993 CBP	1994 CBP	1995 CBP	1996 CBP	1997 CBP	1998 CBP	1999 CBP	2000 CBP	2001 CBP	2002 CBP	2003 CBP	2004 CBP	2005 CBP	2006 CBP	2007 CBP	2008 CBP	2009 CBP	2010 CBP	2011 CBP	2012 CBP	2013 CBP	2014 CBP	2015 CBP	2016 CBP	2017 CBP	2018 CBP	2019 CBP	
- Percent Retail/Transportation																															
- Percent Professional Services																															
- Percent Health Care/Accommodation/Food/Other Services																															

Notes: PEP: US Census Bureau Population Estimates Program

ACS: 5-year American Community Survey

Census: Decennial Census

BLS: Bureau of Labor Statistics

CBP: County Business Patterns

When necessary, rates are calculated using relevant population from the Population Estimates Program.

Interpolated values are a linear interpolation between the preceding and following measured value.

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Appendix 4: Exhibit Notes

Exhibit 1

Timeline of Opioid Shipments and Mortality in the U.S.

1. Shipments panel based on annual ARCOS shipments data covering all states in U.S. from 1997-2019.
2. Shipments are in Morphine Milligram Equivalents (MMEs).
3. Overdose deaths panel based on annual NCHS Mortality Data for the U.S. from 1993 to 2019.
4. Mortality counts are adjusted to allocate unclassified overdoses based on procedures described in Appendix 3.

Exhibit 2

Mortality Rate from Opioid Use Disorder

By Country, 1990-2017

1. Based on annual country-level data in years 1990 through 2017 from the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease Study 2017.
2. Mortality rate is per 100,000.

Exhibit 3

Relationship Between Opioid Shipments and Harms

1. Defendants are individually and collectively responsible for excessive shipments.
2. List of harms are representative and not intended to be comprehensive.

Exhibit 4

Shipments of Prescription Opioids in the U.S.: 1997-2019

By Major Type

1. Based on quarterly ARCOS county data covering all states in the U.S. from 1997Q1 to 2019Q4.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.
3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. Adult population data for 2019 was unavailable; 2018 data was used to calculate MMEs per capita for 2019.
5. MMEs per capita per day are calculated by dividing the MME for each quarter by the adult population and number of days in each quarter.
6. See Appendix 3 for additional details on the ARCOS data.

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Exhibit 5

Shipments of Prescription Opioids in the U.S.: 1997-2010 Average

1. Based on quarterly ARCOS state data, covering all states in the U.S from 1997Q1 to 2010Q4.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.
3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. MMEs per capita per day are calculated by dividing the MME total (after adding the quarterly data) by adult population and 365 days.
5. The map was created using the state 2010 maptile outline.
6. See Appendix 3 for additional details on the ARCOS data.

Exhibit 6

Changes in the Distribution of Per Capita Opioid Shipments Across States: 1997 and 2010

1. Based on quarterly ARCOS state data covering all states in the U.S. for 1997 and 2010.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.
3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. MMEs per capita per day are calculated by dividing the MME total (after adding the quarterly data) by adult population and 365 days.
5. See Appendix 3 for additional details on the ARCOS data.

Exhibit 7

NSDUH Survey Data Indicate that Most Recent Pain Reliever Misuse Is Diversion from Friend, Relative, or Dealer

1. Based on NSDUH annual surveys from 2010.
2. Respondents are surveyed nationally.
3. Limited to people who misused prescription pain relievers within the past year.

Exhibit 8

Opioid Mortality Rate by Type: 1999-2010

U.S. Total

1. Based on monthly NCHS Mortality Data and US Census Data covering all the states in the U.S. from 1999 to 2010.
2. Mortality is opioid related deaths per 100,000 adult population split into prescription related and any illicit opioid related deaths.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

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Exhibit 9

Any Opioid Mortality Rates: 2010

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. in 2010.
2. Mortality is any opioid related deaths per 100,000 adult population.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 10

Shipments and Prescription Opioid Mortality

U.S. Total

1. Based on quarterly ARCOS state data, covering all states in the U.S for 1997, 1999, 2010, and 2019.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.
3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. MMEs per capita per day are calculated by dividing the MME total (after adding the quarterly data) by adult population and 365 days.
5. Mortality based on monthly NCHS Mortality Data and US Census Data covering all the states in the U.S. from 1997, 1999, 2010, and 2019.
6. Mortality is prescription opioid related deaths per 100,000.
7. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
8. See Appendix 3 for additional details on the NCHS, ARCOS and Census data.

Exhibit 11

Prescription and Illicit Opioid Mortality Rate: 1999-2019

U.S. Total

1. Based on monthly NCHS Mortality Data and U.S. Census Data covering all the states in the U.S. from 1999 to 2019.
2. Mortality is opioid related deaths per 100,000 adult population split into prescription related (excluding fentanyl), heroin related (excluding fentanyl), and any fentanyl related deaths.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 12

Shipments and Opioid Mortality

U.S. Total

1. Based on quarterly ARCOS state data, covering all states in the U.S for 1997, 1999, 2010, and 2019.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.

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3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. MMEs per capita per day are calculated by dividing the MME total (after adding the quarterly data) by adult population and 365 days.
5. Mortality based on monthly NCHS Mortality Data and US Census Data covering all the states in the U.S. from 1997, 1999, 2010, and 2019.
6. Mortality is any opioid related deaths per 100,000.
7. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
8. See Appendix 3 for additional details on the NCHS, ARCOS and Census data.

Exhibit 13

Share of Drug Confiscations Identified Involving Illicit Opioids

2010-2018

1. Based on annual state level confiscation data from the U.S. DEA, Diversion Control Division covering all states from 2010 to 2018.
2. Data aggregated to national level and calculated as share of total confiscations.
3. Share reflects heroin and fentanyl substances included in top 60 NFLIS substances identified divided by the identified top 60 substances.
4. See Appendix 3 for additional details on the NFLIS data.

Exhibit 14

Illicit Opioid Mortality Rates: 2019

1. Based on 2019 NCHS Mortality Data and U.S. Census Data covering all the states in the U.S.
2. Mortality is any illicit opioid related deaths per 100,000 adult population.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 15

Illicit Opioid Mortality Rate: 2010-2019

Eastern States vs. Western States

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 2010 to 2019.
2. Western States are defined as the 24 states west of the Mississippi River including Alaska and Hawaii.
3. Mortality is any illicit opioid related deaths per 100,000 adult population.
4. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
5. See Appendix 3 for additional details on the NCHS and Census data.

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Exhibit 16

**Share of Drug Confiscations Identified in NFLIS Involving Illicit Opioids
Eastern States vs. Western States**

1. Based on annual confiscation data from the U.S. DEA, Diversion Control Division covering all states from 2010 to 2018.
2. West coast states are defined as the 24 states west of the Mississippi River including Alaska and Hawaii.
3. Share reflects heroin and fentanyl substances included in top 60 NFLIS substances identified divided by the identified top 60 substances.
4. See Appendix 3 for additional details on the NFLIS data.

Exhibit 17

Measures of U.S. Opioid-Related Disorder

1. Based on NSDUH 4-Year Restricted-use Data Analysis System (RDAS) survey averages from 2006-2009 and 2015-2018.
2. Respondents are surveyed nationally.
3. The 4-year NSDUH averages are used to reduce state-level variation due to small sample size.
4. 2006-2009 Opioid Use Disorder defined as those with either Heroin or RX Use Disorder.

Exhibit 18

National NAS Hospitalization Rate

1. Based on HCUP annual data from 2008-2017.
2. 2008-2014 data are based on ICD-9 while 2016-2018 are based on ICD-10.

Exhibit 19

National Opioid-Related Emergency Department Visit Rate

1. Based on HCUP annual data from 2006-2017.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.

Exhibit 20

National Opioid-Related Inpatient Stay Rate

1. Based on HCUP annual data from 2006-2017.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.

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Exhibit 21

National Rate of Children in Foster Care

1. Based on AFCARS annual data from 2005-2019.
2. United States data is calculated as the national average foster care placement weighted by child population.

Exhibit 22

Total Opioid Mortality Rate: 1993-2019

High vs. Low Shipment States

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1993 to 2019.
2. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.
3. Mortality is any illicit opioid related deaths per 100,000 adult population.
4. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
5. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 23

Prescription Opioid Mortality Rate: 1999-2019

High vs. Low Shipment States

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2019.
2. High, and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.
3. Mortality is prescription opioid related deaths per 100,000 adult population.
4. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
5. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 24

Illicit Opioid Mortality Rate: 1999-2019

High vs. Low Shipment States

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2019.
2. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

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3. Mortality is illicit opioid related deaths per 100,000 adult population.
4. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
5. See Appendix 3 for additional details on the NCHS and Census data.
6. Exhibit 8

Exhibit 25

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Change in Opioid-Related Mortality through 2010

1. Shipments variable is calculated as the 1997-2010 average from quarterly ARCOS state data.
2. Mortality data is based on annual NCHS Mortality Data from 1993 to 2010.
3. Control variables are from the U.S. Census Data covering all states in the U.S.
4. Excludes DC and Puerto Rico.
5. But-For mortality based on assumption that shipments remain at 1997 levels.

Exhibit 26

Structural Change in Prescription Opioid Mortality in January 2011

1. Based on NCHS national mortality data from 1999-2019.
2. Break point identified based on maximum value of F-test of equivalence of trends and intercepts.
3. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 27

Structural Change in Heroin Mortality in December 2010

1. Based on NCHS national mortality data from 1999-2015.
2. Break point identified based on maximum value of F-test of equivalence of trends and intercepts.
3. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 28

Structural Change in Fentanyl Mortality in October 2014

1. Based on NCHS national mortality data from 1999-2019.
2. Break point identified based on maximum value of F-test of equivalence of trends and intercepts.
3. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 29

Structural Change in Illicit Opioid Mortality

High vs. Low Shipment States

1. Based on NCHS state mortality data from 1999-2019.
2. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME,

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MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

3. Break point identified based on maximum value of F-test of equivalence of trends and intercepts.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 30

Actual and Predicted Opioid Mortality Rate in 2009-19

Based on Determinants of Opioid Mortality in 2009-10

1. Mortality data is based on annual NCHS Mortality Data from 2009 to 2019.
2. Control variables are from the U.S. Census Data covering all states in the U.S.
3. Excludes DC and Puerto Rico.
4. Indirect regression estimates for any opioid mortality in 2009-10 are used to generate the predicted mortality for years 2009-2019.

Exhibit 31

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Change in Opioid-Related Mortality through 2019

1. Shipments variable is calculated as the 1997-2010 average from quarterly ARCOS state data.
2. Mortality data is based on annual NCHS Mortality Data from 1993 to 2019.
3. Control variables are from the U.S. Census Data covering all states in the U.S.
4. Excludes DC and Puerto Rico.
5. But-For mortality based on assumption that shipments remain at 1997 levels.

Exhibit 32

NSDUH Opioid Use Disorder Rate

High vs. Low Shipment States

1. Based on NSDUH 2-Year Restricted-use Data Analysis System (RDAS) survey averages from 2002-2019 and charted as mid-point of two-year range.
2. High and low shipments states are aggregated by taking the weighted average of the opioid use disorder rate by total population.
3. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.
4. NSDUH revised questions regarding pain reliever use/abuse in 2015. The dotted lines reflect this revision.

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Exhibit 33

NSDUH Heroin Use Disorder Rate

High vs. Low Shipment States

1. Based on NSDUH 2-Year Restricted-use Data Analysis System (RDAS) survey averages from 2002 to 2019 and charted as mid-point of two-year range.
2. High and low shipments states are aggregated by taking the weighted average of the heroin use disorder rate by total population.
3. High, and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.
4. NSDUH revised questions regarding pain reliever use/abuse in 2015. Questions regarding heroin use/abuse are unaffected by this change.

Exhibit 34

NAS Hospitalization Rate

High vs. Low Shipment States

1. Based on HCUP annual data from 2008-2018.
2. 2008-2014 data are based on ICD-9 while 2016-2018 are based on ICD-10. Full statistics are not available for 2015 because the ICD-9 to ICD-10 transition occurred on 10/01/2015.
3. High and low shipments states are aggregated by taking the weighted average of the NAS newborn rate by the number of child hospitalizations.
4. High, and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

Exhibit 35

Opioid-Related Emergency Department Visit Rate

High vs. Low Shipment States

1. Based on HCUP annual data from 2006-2018.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
3. High and low shipments states are aggregated by taking the weighted average of emergency department visits by total population from the Census Data.
4. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME,

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MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

Exhibit 36

Opioid-Related Inpatient Stay Rate

High vs. Low Shipment States

1. Based on HCUP annual data from 2006-2018.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.
3. High and low shipments states are aggregated by taking the weighted average of inpatient visits by total population from the Census Data.
4. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

Exhibit 37

Rate of Children in Foster Care

High vs. Low Shipment States

1. Based on AFCARS annual data from 2005-2019.
2. High and low shipments states are aggregated by taking the weighted average of childcare rate by total population (ages 0-19).
3. High and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.

Exhibit 38

Regression Estimates of the Relationship between Shipments of Prescription Opioids and Changes in Non-Mortality Harms

1. Shipments variable is calculated as the 1997-2010 average from quarterly ARCOS state data.
2. Opioid Use Disorder Rate and Heroin Use Disorder Rate are based on NSDUH 2-Year Restricted-use Data Analysis System (RDAS) survey averages from 2002 to 2019 and charted as end-of-year.
3. NAS Hospitalization Rate, Emergency Department Visit Rate, and Inpatient Stay Rate are based on HCUP annual data from 2006 to 2018.
4. Rate of Children in Foster Care is based on AFCARS annual data from 2010 to 2019.
5. Control variables are from the Census Data covering all states in the U.S.

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6. NAS is measured as rate per 1,000 hospital births; other metrics measured as rate per 100,000 state residents.

Exhibit 39

“Deaths of Despair” Mortality Rates: 1993-2019

U.S. Total

1. Based on annual NCHS Mortality Data and Census Data covering all states in the U.S. from 1993 to 2019.
2. Mortality is calculated as deaths per 100,000 adult population split into any opioid related deaths, non-opioid overdoses, non-opioid suicides, and alcohol-related liver disease deaths.
3. Despair categories defined based on work papers from Case and Deaton.
4. Mortality rates are calculated using adult population (age 15+) from the Census Data.
5. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 40

Mortality Rate by “Deaths of Despair” Category and State Shipment Level

Change in Mortality Rate Relative to 1993-95 Average

1. Based on annual NCHS Mortality Data and Census Data covering all states in the U.S. from 1993 to 2018.
2. High, and low shipment states are identified as states comprising of the top and bottom 25% of U.S. population, respectively. High shipment states are: AK, AZ, DE, FL, KY, ME, MO, NV, PA, OH, OK, OR, TN, WV; low shipments states are: DC, HI, IA, IL, MN, ND, NE, NY, SD, TX.
3. Mortality is calculated as deaths per 100,000 adult population split into any opioid related deaths, non-opioid overdoses, non-opioid suicides, and alcohol-related liver disease deaths.
4. Despair categories defined based on work papers from Case and Deaton.
5. Mortality rates are calculated using adult population (age 15+) from the Census Data.
6. Mortality Rates are calculated as the change in mortality rate relative to the average between 1993 and 1995.
7. See Appendix 3 for additional details on the NCHS and Census Data.

Exhibit 41

Shipments of Prescription Opioids: 1997-2019

U.S. Total and Ohio

1. Based on quarterly ARCOS county data covering all counties in the U.S. from 1997Q1 to 2019Q4.
2. Shipments are in Morphine Milligram Equivalents (MMEs).
3. Shipments per capita are calculated using adult population (age 15+) from the Census Data.
4. MMEs per capita per day are calculated by dividing the MME for each quarter by adult population and number of days in each quarter.

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5. See Appendix 3 for additional details on the ARCOS data.

Exhibit 42

Shipments of Prescription Opioids by County: 1997-2010 Average

Comparison to National Average

1. Based on quarterly ARCOS county data covering all counties in the Ohio from 1997Q1 to 2019Q4.
2. Shipments are in Morphine Milligram Equivalents (MMEs).
3. Shipments per capita are calculated using adult population (age 15+) from the Census Data.
4. MMEs per capita per day are calculated by dividing the MME for each quarter by adult population and number of days in each quarter.
5. Ratio calculated between county-level shipments and national shipments per capita per day from 1997-2010.
6. See Appendix 3 for additional details on the ARCOS data.

Exhibit 43

Total Opioid Mortality Rates: 1993-2010

Ohio and U.S. Total

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2010.
2. Mortality is opioid related deaths per 100,000 adult population.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 44

Prescription vs. Illicit Opioid Mortality Rates: 1999-2010

Ohio and U.S. Total

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2010.
2. Mortality is opioid related deaths per 100,000 adult population split into prescription related deaths and illicit opioid related deaths.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 45

Total Opioid Mortality Rates: 1993-2019

Ohio and U.S. Total

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2019.
2. Mortality is opioid related deaths per 100,000 adult population.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.

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4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 46

Prescription vs. Illicit Opioid Mortality Rates: 1999-2019

Ohio and U.S. Total

1. Based on annual NCHS Mortality Data and U.S. Census Data covering all states in the U.S. from 1999 to 2019.
2. Mortality is opioid related deaths per 100,000 adult population split into prescription related deaths and illicit opioid related deaths.
3. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
4. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 47

Share of Drug Confiscations Involving Illicit Opioids

Ohio and U.S. Total

1. Based on annual state level confiscation data from the U.S. DEA, Diversion Control Division covering all states from 2010 to 2018.
2. Data aggregated to national level and calculated as share of total confiscations.
3. Share reflects heroin and fentanyl substances included in top 60 NFLIS substances identified divided by the identified top 60 substances.
4. See Appendix 3 for additional details on the NFLIS data.

Exhibit 48

Shipments and Illicit and Total Opioid Mortality

U.S. and Ohio

1. Based on quarterly ARCOS state and county data, covering all states in the U.S for 1997, 1999, 2010, and 2018.
2. Shipments are in Morphine Milligram Equivalents (MMEs) per capita per day.
3. Shipments per capita are calculated using adult population (age 15+) from the Census Bureau.
4. MMEs per capita per day are calculated by dividing the MME total (after adding the quarterly data) by adult population and 365 days.
5. Mortality based on monthly NCHS Mortality Data and US Census Data covering all the states in the U.S. from 1997, 1999, 2010, and 2019.
6. Mortality is any opioid related deaths per 100,000 and any illicit opioid related deaths per 100,000.
7. Mortality rates are calculated using adult population (age 15+) from the Census Bureau.
8. See Appendix 3 for additional details on the NCHS, ARCOS and Census data.

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Exhibit 49

"Deaths of Despair" Mortality Rates: 1993-2019

1. Based on annual NCHS Mortality Data and Census Data covering all states in the U.S. and from 1993 to 2019 and Ohio from 1993 to 2019.
2. Mortality is calculated as deaths per 100,000 adult population split into any opioid related deaths, non-opioid overdoses, non-opioid suicides, and alcohol-related liver disease deaths.
3. Despair categories defined based on work papers from Case and Deaton.
4. Mortality rates are calculated using adult population (age 15+) from the Census Data.
5. See Appendix 3 for additional details on the NCHS and Census data.

Exhibit 50

Actual and Predicted Opioid Mortality Rates in 2009-2019

Based on Determinants of Opioid Mortality in 2009-2010

1. Mortality data is based on annual NCHS Mortality Data from 2009 to 2019.
2. Control variables are from the U.S. Census Data covering large county sample.
3. Indirect regression estimates for any opioid mortality in 2009-10 are used to generate the predicted mortality for years 2009-2019 based on actual demographic and economic variables for Lake and Trumbull Counties.

Exhibit 51

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019

Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags

1. Flagged MMEs based on analysis of Catizone/McCann.
2. Shipments variable is calculated as the 1997-2010 average from quarterly ARCOS county data.
3. Mortality data is based on any opioid overdose deaths per 100,000 adults (age 15+) from the annual NCHS Mortality Data.
4. Control variables are from the Census Data covering large counties in the U.S.
5. Excludes DC and Puerto Rico.

Exhibit 52

Impact of Defendants on Annual Total Opioid Mortality By Year

Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags

1. Mortality data is based on any opioid overdose deaths per 100,000 adults (age 15+) from the annual NCHS Mortality Data in 1993 to 2019.
2. Mortality attributable to defendants based on analyses of Catizone/McCann and regression analysis described in Exhibit 49.
3. Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

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Exhibit 53

Impact of Defendants on Annual Total Opioid Mortality

Total Number of Deaths Attributable to Defendants, 1996-2019

1. Mortality data is based on any opioid overdose deaths per 100,000 adults (age 15+) from the annual NCHS Mortality Data in 1993 to 2019.
2. Mortality attributable to defendants for 2009-2010 and 2018-2019 based on analyses of Rafalski/Catizone/McCann and regression analyses as described in Exhibit 51.
3. Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

Exhibit 54

Measures of Opioid-Related Disorder

U.S. vs. Ohio

1. Based on NSDUH 4-Year Restricted-use Data Analysis System (RDAS) survey averages from 2006-2009 and 2015-2018.
2. Respondents are surveyed nationally and for Ohio.
3. The 4-year NSDUH averages are used to reduce state-level variation due to small sample size.
4. 2006-2009 Opioid Use Disorder defined as those with either Heroin or RX Use Disorder.

Exhibit 55

NSDUH Survey Data Indicate that Most Recent Pain Reliever Misuse Is Diversion from Friend, Relative, or Dealer

1. Based on NSDUH annual surveys from 2010 as well as the 2-Year Restricted-use Data Analysis System (RDAS) from 2010-2011.
2. Respondents are surveyed nationally and for Ohio.
3. Limited to people who misused prescription pain relievers within the past year.

Exhibit 56

NAS Hospitalization Rate

U.S. vs. Ohio

1. Based on HCUP annual data from 2008-2018.
2. 2008-2014 data are based on ICD-9 while 2016-2018 are based on ICD-10.

Exhibit 57

Opioid-Related Emergency Department Visit Rate

U.S. vs. Ohio

1. Based on HCUP annual data from 2006-2018.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.

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Exhibit 58

Opioid-Related Inpatient Stay Rate

U.S. vs. Ohio

1. Based on HCUP annual data from 2006-2018.
2. Because HCUP data switched from ICD-9 to ICD-10 in 2015Q4, annual rates are calculated for years ending in the 3rd quarter (e.g. 2015 includes 2014Q4 to 2015Q3). The 2006 to 2015 rates are based entirely on the ICD-9 classification system whereas the 2016-2018 rates are based entirely on the ICD-10 classification system.

Exhibit 59

Rate of Children in Foster Care

U.S. vs. Ohio

1. Based on AFCARS annual data from 2005-2018.
2. U.S. data is calculated as the national average for foster care placement weighted by child population.
3. United States data is calculated as the national average foster care placement weighted by child population.

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Appendix 5: Regression Estimates of Determinants of Per Capita Shipments in 2010

Appendix Exhibit 5.1 Relationship between Per Capita Shipments in 2010 and Economic and Demographic Factors: State-Level Analysis

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.18

Variable	Coef.	Std. Err	t	P> t
Shipments per Capita per Day in 2010				
Change in Median Household Income (Thousands) in 2010	0.00	0.02	0.22	0.83
Prime Male Employment to Population in 2010	-9.80	3.14	-3.12	0.00
Percent White in 2010	0.57	0.87	0.66	0.51
Percent Less High School in 2010	-1.31	4.21	-0.31	0.76
Percent Male in 2010	7.41	18.10	0.41	0.68
Percent Under 30 in 2010	-12.35	9.25	-1.33	0.19
Percent 30 to 64 in 2010	-11.65	13.15	-0.89	0.38
Constant	16.74	10.66	1.57	0.12

Source: U.S. Census Data; ARCOS Data.

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Appendix Exhibit 5.2
Relationship between Per Capita Shipments in 2010 and Economic and Demographic Factors:
County-Level Analysis
Large Counties

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.26

Variable	Coef.	Std. Err	t	P> t
Shipments per Capita per Day in 2010				
Percent Male in 2010	-5.32	6.36	-0.84	0.40
Percent Under 15 in 2010	-7.08	3.64	-1.95	0.05
Percent 15 to 29 in 2010	-5.03	3.68	-1.37	0.17
Percent 30 to 44 in 2010	-4.56	4.54	-1.00	0.32
Percent 45 to 64 in 2010	-1.27	5.34	-0.24	0.81
Percent White in 2010	-0.02	0.94	-0.02	0.98
Percent Black in 2010	-1.42	0.98	-1.44	0.15
Percent Hispanic in 2010	-1.22	0.86	-1.41	0.16
Percent Less High School in 2010	0.05	2.39	0.02	0.98
Percent High School in 2010	1.01	1.62	0.62	0.53
Percent Some College in 2010	2.73	2.12	1.29	0.20
Employment Ratio in 2010	-2.58	2.00	-1.29	0.20
Percent Unemployed in 2010	5.37	3.37	1.59	0.11
Median Household Income (Thousands) in 2010	-0.03	0.01	-2.74	0.01
Percent Ag/M/Const/Util in 2010	0.87	1.72	0.51	0.61
Percent Manufacturing in 2010	-2.60	1.11	-2.34	0.02
Percent Retail/Transportation in 2010	1.85	1.28	1.44	0.15
Percent Professional in 2010	3.39	1.37	2.47	0.01
Poverty Rate in 2010	-2.85	3.02	-0.95	0.34
Census Population (Thousands) in 2010	0.00	0.00	-1.34	0.18
Percent Urban in 2010	1.27	0.54	2.38	0.02
Constant	9.17	3.84	2.39	0.02

Source: U.S. Census Data; ARCOS Data.

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Appendix 6: Regression Estimates of the Relationship Between Per Capita Shipments and Change in Opioid-Related Mortality through 2009-2010

Appendix Exhibit 6.1

Relationship between Per Capita Shipments and Change in Opioid Mortality Rate from 1993-1995 to 2009-2010

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.54

Variable	Coef.	Std. Err	t	P> t
Change in Any Opioid Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	8.57	1.48	5.80	0.00
Any Opioid Mortality Rate in 1993-1995	-0.54	0.29	-1.84	0.07
Change in Median Household Income (Thousands) 1993-1995 to 2009-2010	0.14	0.18	0.78	0.44
Change in Prime Male Employment to Population 1993-1995 to 2009-2010	-14.93	18.08	-0.83	0.41
Change in Percent White 1993-1995 to 2009-2010	39.02	26.17	1.49	0.14
Change in Percent Less High School 1993-1995 to 2009-2010	1.59	27.85	0.06	0.95
Change in Census Population (Thousands) 1993-1995 to 2009-2010	2.78	2.74	1.01	0.32
Constant	-1.43	3.24	-0.44	0.66

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

Appendix Exhibit 6.2

Relationship between Per Capita Shipments and Change in Prescription Opioid Mortality Rate from 1999-2000 to 2009-2010

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.46

Variable	Coef.	Std. Err	t	P> t
Change in Prescription Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	5.27	1.18	4.46	0.00
Prescription Opioids Mortality Rate in 1999-2000	0.06	0.21	0.29	0.78
Change in Median Household Income (Thousands) 1999-2000 to 2009-2010	-0.11	0.17	-0.64	0.53
Change in Prime Male Employment to Population 1999-2000 to 2009-2010	14.77	19.13	0.77	0.44
Change in Percent White 1999-2000 to 2009-2010	46.89	27.28	1.72	0.09
Change in Percent Less High School 1999-2000 to 2009-2010	-59.34	39.77	-1.49	0.14
Change in Census Population (Thousands) 1999-2000 to 2009-2010	6.33	3.52	1.80	0.08
Constant	-2.94	2.15	-1.37	0.18

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 6.3
Relationship between Per Capita Shipments and Change in Illicit Opioid Mortality Rate from
1999-2000 to 2009-2010

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.51

Variable	Coef.	Std. Err	t	P> t
Change in Illicit Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	0.30	0.35	0.85	0.40
Illicit Opioids Mortality Rate in 1999-2000	-0.45	0.09	-4.98	0.00
Change in Median Household Income (Thousands) 1999-2000 to 2009-2010	-0.06	0.04	-1.32	0.19
Change in Prime Male Employment to Population 1999-2000 to 2009-2010	-11.56	5.86	-1.97	0.06
Change in Percent White 1999-2000 to 2009-2010	30.34	10.06	3.02	0.00
Change in Percent Less High School 1999-2000 to 2009-2010	18.40	10.54	1.75	0.09
Change in Census Population (Thousands) 1999-2000 to 2009-2010	-3.20	1.87	-1.71	0.09
Constant	1.30	0.66	1.96	0.06

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix 7: Regression Estimates of Determinants of Opioid-Related Mortality as of 2009-2010

Appendix Exhibit 7.1

Relationship between Any Opioid Mortality in 2009-2010 and Economic and Demographic Factors: State-Level Analysis

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.49

Variable	Coef.	Std. Err	t	P> t
Any Opioid Mortality Rate in 2009-2010				
Percent Male in 2009-2010	137.86	70.54	1.95	0.06
Percent Under 30 in 2009-2010	18.46	24.34	0.76	0.45
Median Household Income (Thousands) in 2009-2010	0.16	0.09	1.78	0.08
Prime Male Employment to Population in 2009-2010	-90.26	15.11	-5.97	0.00
Percent White in 2009-2010	13.48	3.39	3.97	0.00
Percent Less High School in 2009-2010	36.70	19.98	1.84	0.07
Census Population (Thousands) in 2009-2010	0.00	0.00	-2.45	0.02
Constant	-11.75	34.09	-0.34	0.73

Source: NCHS Mortality Data; U.S. Census Data.

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Appendix Exhibit 7.2

**Relationship between Any Opioid Mortality in 2009-2010 and Economic and Demographic Factors:
County-Level Analysis**

Large Counties

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.37

Variable	Coef.	Std. Err	t	P> t
Any Opioid Mortality Rate in 2009-2010				
Percent Male in 2009-2010	-24.05	36.37	-0.66	0.51
Percent Under 15 in 2009-2010	-10.76	18.57	-0.58	0.56
Percent 15 to 29 in 2009-2010	21.65	17.89	1.21	0.23
Percent 30 to 44 in 2009-2010	96.81	23.36	4.15	0.00
Percent 45 to 64 in 2009-2010	46.38	31.53	1.47	0.14
Percent White in 2009-2010	17.34	3.54	4.90	0.00
Percent Black in 2009-2010	-9.28	3.83	-2.42	0.02
Percent Hispanic in 2009-2010	-23.68	4.99	-4.75	0.00
Percent Less High School in 2009-2010	35.69	13.84	2.58	0.01
Percent High School in 2009-2010	9.78	7.15	1.37	0.17
Percent Some College in 2009-2010	38.03	12.14	3.13	0.00
Employment Ratio in 2009-2010	-35.03	10.92	-3.21	0.00
Percent Unemployed in 2009-2010	36.37	18.68	1.95	0.05
Median Household Income (Thousands) in 2009-2010	-0.06	0.06	-0.97	0.33
Percent Ag/M/Const/Util in 2009-2010	30.34	10.21	2.97	0.00
Percent Manufacturing in 2009-2010	-13.85	8.01	-1.73	0.08
Percent Retail/Transportation in 2009-2010	-8.60	10.24	-0.84	0.40
Percent Professional in 2009-2010	0.23	5.58	0.04	0.97
Poverty Rate in 2009-2010	8.01	15.43	0.52	0.60
Census Population (Thousands) in 2009-2010	0.00	0.00	-1.64	0.10
Percent Urban in 2009-2010	20.85	3.04	6.87	0.00
Constant	-33.89	23.50	-1.44	0.15

Source: NCHS Mortality Data; U.S. Census Data.

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Appendix 8: Regression Estimates of the Relationship Between Per Capita Shipments and Change in Opioid-Related Morality through 2018-2019

Appendix Exhibit 8.1

Relationship between Per Capita Shipments and Change in Illicit Opioid Mortality Rate from 2009-2010 to 2018-2019

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.38

Variable	Coef.	Std. Err	t	P> t
Change in Illicit Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	10.69	3.71	2.88	0.01
Illicit Opioids Mortality Rate in 2009-2010	1.72	1.18	1.45	0.15
Change in Median Household Income (Thousands) 2009-2010 to 2018-2019	0.56	0.80	0.70	0.49
Change in Prime Male Employment to Population 2009-2010 to 2018-2019	53.36	43.23	1.23	0.22
Change in Percent White 2009-2010 to 2018-2019	-292.59	139.50	-2.10	0.04
Change in Percent Less High School 2009-2010 to 2018-2019	-110.31	112.16	-0.98	0.33
Change in Census Population (Thousands) 2009-2010 to 2018-2019	-112.22	22.02	-5.10	0.00
Constant	-11.19	6.23	-1.80	0.08

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

Appendix Exhibit 8.2

Relationship between Per Capita Shipments and Change in Any Opioid Mortality Rate from 1993-1995 to 2018-2019

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.46

Variable	Coef.	Std. Err	t	P> t
Change in Any Opioid Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	13.16	4.37	3.01	0.00
Any Opioid Mortality Rate in 1993-1995	-0.02	0.60	-0.04	0.97
Change in Median Household Income (Thousands) 1993-1995 to 2018-2019	-0.72	0.29	-2.50	0.02
Change in Prime Male Employment to Population 1993-1995 to 2018-2019	174.58	68.80	2.54	0.02
Change in Percent White 1993-1995 to 2018-2019	-64.46	70.24	-0.92	0.36
Change in Percent Less High School 1993-1995 to 2018-2019	-84.82	41.59	-2.04	0.05
Change in Census Population (Thousands) 1993-1995 to 2018-2019	-16.95	5.75	-2.95	0.01
Constant	-5.01	9.30	-0.54	0.59

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix 9: Regression Estimates of the Relationship Between Per Capita Shipments and Opioid-Related Mortality Based on County-Level Data

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Appendix Exhibit 9.1

Relationship between Per Capita Shipments and Change in Opioid Mortality Rate from
1993-1995 to 2009-2010*Large Counties*

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.58

Variable	Coef.	Std. Err	t	P> t
Change in Any Opioid Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	4.04	0.48	8.46	0.00
Any Opioid Mortality Rate in 1993-1995	-0.81	0.12	-7.03	0.00
Percent Male in 1993-1995	2.68	40.29	0.07	0.95
Percent Under 15 in 1993-1995	0.30	23.01	0.01	0.99
Percent 15 to 29 in 1993-1995	22.06	21.37	1.03	0.30
Percent 30 to 44 in 1993-1995	97.88	23.75	4.12	0.00
Percent 45 to 64 in 1993-1995	33.27	54.35	0.61	0.54
Percent White in 1993-1995	7.99	3.34	2.40	0.02
Percent Black in 1993-1995	-14.49	4.16	-3.48	0.00
Percent Hispanic in 1993-1995	-16.98	4.78	-3.56	0.00
Percent Less High School in 1993-1995	20.08	14.38	1.40	0.16
Percent High School in 1993-1995	18.49	10.49	1.76	0.08
Percent Some College in 1993-1995	45.52	15.13	3.01	0.00
Employment Ratio in 1993-1995	-27.80	10.71	-2.60	0.01
Percent Unemployed in 1993-1995	22.96	22.82	1.01	0.32
Median Household Income (Thousands) in 1993-1995	0.04	0.06	0.78	0.43
Percent Ag/M/Const/Util in 1993-1995	26.44	11.23	2.35	0.02
Percent Manufacturing in 1993-1995	-11.81	8.03	-1.47	0.14
Percent Retail/Transportation in 1993-1995	-13.31	8.60	-1.55	0.12
Percent Professional in 1993-1995	0.27	5.89	0.05	0.96
Poverty Rate in 1993-1995	27.14	15.83	1.71	0.09
Census Population (Thousands) in 1993-1995	0.00	0.00	0.42	0.68
Percent Urban in 1993-1995	16.01	3.17	5.06	0.00
Change in Percent Male 1993-1995 to 2009-2010	-21.56	78.74	-0.27	0.78
Change in Percent Under 15 1993-1995 to 2009-2010	60.80	44.71	1.36	0.17
Change in Percent 15 to 29 1993-1995 to 2009-2010	63.97	49.69	1.29	0.20
Change in Percent 30 to 44 1993-1995 to 2009-2010	118.14	66.15	1.79	0.07
Change in Percent 45 to 64 1993-1995 to 2009-2010	83.24	61.76	1.35	0.18
Change in Percent White 1993-1995 to 2009-2010	51.77	12.68	4.08	0.00
Change in Percent Black 1993-1995 to 2009-2010	36.98	14.26	2.59	0.01
Change in Percent Hispanic 1993-1995 to 2009-2010	-14.69	11.34	-1.29	0.20
Change in Percent Less High School 1993-1995 to 2009-2010	-5.46	25.84	-0.21	0.83
Change in Percent High School 1993-1995 to 2009-2010	26.79	18.21	1.47	0.14
Change in Percent Some College 1993-1995 to 2009-2010	-7.60	31.91	-0.24	0.81
Change in Employment Ratio 1993-1995 to 2009-2010	-44.25	14.72	-3.01	0.00
Change in Percent Unemployed 1993-1995 to 2009-2010	20.93	25.01	0.84	0.40
Change in Median Household Income (Thousands) 1993-1995 to 2009-2010	0.10	0.10	0.94	0.35
Change in Percent Ag/M/Const/Util 1993-1995 to 2009-2010	38.78	16.08	2.41	0.02
Change in Percent Manufacturing 1993-1995 to 2009-2010	-8.43	13.69	-0.62	0.54
Change in Percent Retail/Transportation 1993-1995 to 2009-2010	19.36	21.19	0.91	0.36
Change in Percent Professional 1993-1995 to 2009-2010	3.43	10.25	0.33	0.74
Change in Poverty Rate 1993-1995 to 2009-2010	8.12	22.42	0.36	0.72
Change in Census Population (Thousands) 1993-1995 to 2009-2010	0.00	0.00	-2.10	0.04
Change in Percent Urban 1993-1995 to 2009-2010	11.43	6.24	1.83	0.07
Constant	-52.58	30.59	-1.72	0.09

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 9.2

Relationship between Per Capita Shipments and Change in Prescription Opioid Mortality Rate from 1999-2000 to 2009-2010

Large Counties

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.48

Variable	Coef.	Std. Err	t	P> t
Change in Prescription Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	2.37	0.37	6.41	0.00
Prescription Opioids Mortality Rate in 1999-2000	-0.47	0.09	-5.41	0.00
Percent Male in 1999-2000	10.16	26.48	0.38	0.70
Percent Under 15 in 1999-2000	1.52	13.92	0.11	0.91
Percent 15 to 29 in 1999-2000	10.13	11.42	0.89	0.38
Percent 30 to 44 in 1999-2000	39.80	15.47	2.57	0.01
Percent 45 to 64 in 1999-2000	23.51	23.94	0.98	0.33
Percent White in 1999-2000	5.24	2.67	1.96	0.05
Percent Black in 1999-2000	-5.18	2.98	-1.74	0.08
Percent Hispanic in 1999-2000	-6.64	2.23	-2.98	0.00
Percent Less High School in 1999-2000	8.70	8.81	0.99	0.32
Percent High School in 1999-2000	8.84	5.22	1.69	0.09
Percent Some College in 1999-2000	20.31	7.68	2.65	0.01
Employment Ratio in 1999-2000	-20.30	6.37	-3.19	0.00
Percent Unemployed in 1999-2000	-16.93	15.27	-1.11	0.27
Median Household Income (Thousands) in 1999-2000	0.01	0.04	0.15	0.88
Percent Ag/M/Const/Util in 1999-2000	15.77	6.66	2.37	0.02
Percent Manufacturing in 1999-2000	-6.84	5.02	-1.36	0.17
Percent Retail/Transportation in 1999-2000	-2.33	4.77	-0.49	0.63
Percent Professional in 1999-2000	0.39	3.35	0.12	0.91
Poverty Rate in 1999-2000	6.17	9.74	0.63	0.53
Census Population (Thousands) in 1999-2000	0.00	0.00	-0.40	0.69
Percent Urban in 1999-2000	6.29	1.86	3.38	0.00
Change in Percent Male 1999-2000 to 2009-2010	47.06	66.13	0.71	0.48
Change in Percent Under 15 1999-2000 to 2009-2010	53.13	34.78	1.53	0.13
Change in Percent 15 to 29 1999-2000 to 2009-2010	29.99	32.36	0.93	0.35
Change in Percent 30 to 44 1999-2000 to 2009-2010	103.38	41.34	2.50	0.01
Change in Percent 45 to 64 1999-2000 to 2009-2010	75.25	40.17	1.87	0.06
Change in Percent White 1999-2000 to 2009-2010	30.78	10.72	2.87	0.00
Change in Percent Black 1999-2000 to 2009-2010	17.64	14.04	1.26	0.21
Change in Percent Hispanic 1999-2000 to 2009-2010	-5.78	9.84	-0.59	0.56
Change in Percent Less High School 1999-2000 to 2009-2010	14.18	16.72	0.85	0.40
Change in Percent High School 1999-2000 to 2009-2010	22.31	14.15	1.58	0.12
Change in Percent Some College 1999-2000 to 2009-2010	-1.84	19.62	-0.09	0.93
Change in Employment Ratio 1999-2000 to 2009-2010	-37.29	10.98	-3.40	0.00
Change in Percent Unemployed 1999-2000 to 2009-2010	-6.50	17.55	-0.37	0.71
Change in Median Household Income (Thousands) 1999-2000 to 2009-2010	0.11	0.06	1.74	0.08
Change in Percent Ag/M/Const/Util 1999-2000 to 2009-2010	29.66	11.09	2.67	0.01
Change in Percent Manufacturing 1999-2000 to 2009-2010	-3.30	10.84	-0.30	0.76
Change in Percent Retail/Transportation 1999-2000 to 2009-2010	14.72	9.82	1.50	0.13
Change in Percent Professional 1999-2000 to 2009-2010	1.72	7.69	0.22	0.82
Change in Poverty Rate 1999-2000 to 2009-2010	15.85	13.38	1.19	0.24
Change in Census Population (Thousands) 1999-2000 to 2009-2010	0.00	0.00	-1.06	0.29
Change in Percent Urban 1999-2000 to 2009-2010	6.02	6.49	0.93	0.35
Constant	-22.54	16.90	-1.33	0.18

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 9.3

Relationship between Per Capita Shipments and Change in Illicit Opioid Mortality Rate from
1999-2000 to 2009-2010*Large Counties*

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.40

Variable	Coef.	Std. Err	t	P> t
Change in Illicit Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	0.50	0.31	1.61	0.11
Illicit Opioids Mortality Rate in 1999-2000	-0.62	0.05	-11.68	0.00
Percent Male in 1999-2000	4.08	15.50	0.26	0.79
Percent Under 15 in 1999-2000	12.03	9.97	1.21	0.23
Percent 15 to 29 in 1999-2000	18.91	8.41	2.25	0.03
Percent 30 to 44 in 1999-2000	30.18	10.82	2.79	0.01
Percent 45 to 64 in 1999-2000	20.83	14.97	1.39	0.17
Percent White in 1999-2000	4.10	1.68	2.44	0.02
Percent Black in 1999-2000	-0.13	1.99	-0.07	0.95
Percent Hispanic in 1999-2000	-2.39	2.39	-1.00	0.32
Percent Less High School in 1999-2000	9.43	6.53	1.44	0.15
Percent High School in 1999-2000	3.67	4.21	0.87	0.38
Percent Some College in 1999-2000	7.01	6.27	1.12	0.26
Employment Ratio in 1999-2000	-7.76	4.20	-1.85	0.07
Percent Unemployed in 1999-2000	-1.73	9.81	-0.18	0.86
Median Household Income (Thousands) in 1999-2000	0.06	0.03	1.76	0.08
Percent Ag/M/Const/Util in 1999-2000	6.54	4.65	1.41	0.16
Percent Manufacturing in 1999-2000	-1.53	2.54	-0.60	0.55
Percent Retail/Transportation in 1999-2000	-6.25	3.79	-1.65	0.10
Percent Professional in 1999-2000	-0.36	2.36	-0.15	0.88
Poverty Rate in 1999-2000	3.14	8.09	0.39	0.70
Census Population (Thousands) in 1999-2000	0.00	0.00	-0.56	0.58
Percent Urban in 1999-2000	4.81	1.30	3.70	0.00
Change in Percent Male 1999-2000 to 2009-2010	52.09	39.32	1.32	0.19
Change in Percent Under 15 1999-2000 to 2009-2010	-14.81	23.39	-0.63	0.53
Change in Percent 15 to 29 1999-2000 to 2009-2010	22.05	19.92	1.11	0.27
Change in Percent 30 to 44 1999-2000 to 2009-2010	63.95	24.86	2.57	0.01
Change in Percent 45 to 64 1999-2000 to 2009-2010	53.86	23.13	2.33	0.02
Change in Percent White 1999-2000 to 2009-2010	27.20	7.92	3.43	0.00
Change in Percent Black 1999-2000 to 2009-2010	26.72	10.17	2.63	0.01
Change in Percent Hispanic 1999-2000 to 2009-2010	-17.29	7.49	-2.31	0.02
Change in Percent Less High School 1999-2000 to 2009-2010	0.00	14.40	0.00	1.00
Change in Percent High School 1999-2000 to 2009-2010	-3.51	9.03	-0.39	0.70
Change in Percent Some College 1999-2000 to 2009-2010	4.38	14.43	0.30	0.76
Change in Employment Ratio 1999-2000 to 2009-2010	-5.23	6.52	-0.80	0.42
Change in Percent Unemployed 1999-2000 to 2009-2010	3.42	10.66	0.32	0.75
Change in Median Household Income (Thousands) 1999-2000 to 2009-2010	-0.04	0.05	-0.87	0.38
Change in Percent Ag/M/Const/Util 1999-2000 to 2009-2010	11.37	8.78	1.29	0.20
Change in Percent Manufacturing 1999-2000 to 2009-2010	2.95	6.00	0.49	0.62
Change in Percent Retail/Transportation 1999-2000 to 2009-2010	12.18	10.37	1.17	0.24
Change in Percent Professional 1999-2000 to 2009-2010	4.53	4.97	0.91	0.36
Change in Poverty Rate 1999-2000 to 2009-2010	20.42	9.95	2.05	0.04
Change in Census Population (Thousands) 1999-2000 to 2009-2010	0.00	0.00	-0.66	0.51
Change in Percent Urban 1999-2000 to 2009-2010	10.30	5.05	2.04	0.04
Constant	-28.01	10.05	-2.79	0.01

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 9.4

Relationship between Per Capita Shipments and Change in Illicit Opioid Mortality Rate from
2009-2010 to 2018-2019*Large Counties*

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.50

Variable	Coef.	Std. Err	t	P> t
Change in Illicit Opioids Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	4.01	1.29	3.11	0.00
Illicit Opioids Mortality Rate in 2009-2010	0.93	0.37	2.51	0.01
Percent Male in 2009-2010	-13.01	94.20	-0.14	0.89
Percent Under 15 in 2009-2010	-9.20	43.97	-0.21	0.83
Percent 15 to 29 in 2009-2010	52.17	38.89	1.34	0.18
Percent 30 to 44 in 2009-2010	-21.03	58.87	-0.36	0.72
Percent 45 to 64 in 2009-2010	120.87	68.81	1.76	0.08
Percent White in 2009-2010	5.91	8.33	0.71	0.48
Percent Black in 2009-2010	17.56	11.10	1.58	0.11
Percent Hispanic in 2009-2010	-20.87	9.31	-2.24	0.03
Percent Less High School in 2009-2010	28.46	31.33	0.91	0.36
Percent High School in 2009-2010	53.47	19.67	2.72	0.01
Percent Some College in 2009-2010	-73.57	28.48	-2.58	0.01
Employment Ratio in 2009-2010	34.58	22.89	1.51	0.13
Percent Unemployed in 2009-2010	273.77	69.18	3.96	0.00
Median Household Income (Thousands) in 2009-2010	0.06	0.13	0.43	0.67
Percent Ag/M/Const/Util in 2009-2010	-71.79	26.68	-2.69	0.01
Percent Manufacturing in 2009-2010	-54.07	14.75	-3.67	0.00
Percent Retail/Transportation in 2009-2010	-38.38	20.61	-1.86	0.06
Percent Professional in 2009-2010	-21.12	14.25	-1.48	0.14
Poverty Rate in 2009-2010	-39.57	39.62	-1.00	0.32
Census Population (Thousands) in 2009-2010	0.00	0.00	0.33	0.74
Percent Urban in 2009-2010	13.85	7.28	1.90	0.06
Change in Percent Male 2009-2010 to 2018-2019	105.32	253.87	0.41	0.68
Change in Percent Under 15 2009-2010 to 2018-2019	-52.66	110.69	-0.48	0.63
Change in Percent 15 to 29 2009-2010 to 2018-2019	-58.55	103.04	-0.57	0.57
Change in Percent 30 to 44 2009-2010 to 2018-2019	-183.96	110.82	-1.66	0.10
Change in Percent 45 to 64 2009-2010 to 2018-2019	39.81	119.64	0.33	0.74
Change in Percent White 2009-2010 to 2018-2019	-17.95	57.52	-0.31	0.76
Change in Percent Black 2009-2010 to 2018-2019	-82.61	80.32	-1.03	0.30
Change in Percent Hispanic 2009-2010 to 2018-2019	109.90	49.85	2.20	0.03
Change in Percent Less High School 2009-2010 to 2018-2019	-377.75	101.85	-3.71	0.00
Change in Percent High School 2009-2010 to 2018-2019	-140.94	53.70	-2.62	0.01
Change in Percent Some College 2009-2010 to 2018-2019	-211.69	65.11	-3.25	0.00
Change in Employment Ratio 2009-2010 to 2018-2019	77.25	28.65	2.70	0.01
Change in Percent Unemployed 2009-2010 to 2018-2019	281.79	86.14	3.27	0.00
Change in Median Household Income (Thousands) 2009-2010 to 2018-2019	-0.53	0.27	-2.00	0.05
Change in Percent Ag/M/Const/Util 2009-2010 to 2018-2019	-1.71	47.67	-0.04	0.97
Change in Percent Manufacturing 2009-2010 to 2018-2019	-26.81	32.55	-0.82	0.41
Change in Percent Retail/Transportation 2009-2010 to 2018-2019	-28.68	34.12	-0.84	0.40
Change in Percent Professional 2009-2010 to 2018-2019	34.77	31.28	1.11	0.27
Change in Poverty Rate 2009-2010 to 2018-2019	-42.02	51.13	-0.82	0.41
Change in Census Population (Thousands) 2009-2010 to 2018-2019	-0.01	0.01	-1.12	0.26
Change in Percent Urban 2009-2010 to 2018-2019	-616.57	540.31	-1.14	0.25
Constant	-62.80	49.78	-1.26	0.21

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 9.5

Relationship between Per Capita Shipments and Change in Any Opioid Mortality Rate from
1993-1995 to 2018-2019*Large Counties*

Ordinary Least Squares Regression

Number of obs = 405

Robust Standard Errors

Adjusted R-squared = 0.55

Variable	Coef.	Std. Err	t	P> t
Change in Any Opioid Mortality Rate				
Avg. Shipments per Capita per Day (1997-2010)	7.47	1.29	5.77	0.00
Any Opioid Mortality Rate in 1993-1995	-0.58	0.25	-2.32	0.02
Percent Male in 1993-1995	-17.71	113.21	-0.16	0.88
Percent Under 15 in 1993-1995	2.20	51.91	0.04	0.97
Percent 15 to 29 in 1993-1995	14.59	44.11	0.33	0.74
Percent 30 to 44 in 1993-1995	-7.37	54.98	-0.13	0.89
Percent 45 to 64 in 1993-1995	-110.85	110.68	-1.00	0.32
Percent White in 1993-1995	5.53	17.62	0.31	0.75
Percent Black in 1993-1995	0.48	19.09	0.03	0.98
Percent Hispanic in 1993-1995	-26.02	10.77	-2.42	0.02
Percent Less High School in 1993-1995	62.42	34.59	1.80	0.07
Percent High School in 1993-1995	76.80	24.24	3.17	0.00
Percent Some College in 1993-1995	-25.40	31.09	-0.82	0.41
Employment Ratio in 1993-1995	23.76	24.14	0.98	0.33
Percent Unemployed in 1993-1995	282.28	86.44	3.27	0.00
Median Household Income (Thousands) in 1993-1995	0.08	0.15	0.54	0.59
Percent Ag/M/Const/Util in 1993-1995	-22.17	23.92	-0.93	0.35
Percent Manufacturing in 1993-1995	-40.78	14.19	-2.87	0.00
Percent Retail/Transportation in 1993-1995	-47.00	23.47	-2.00	0.05
Percent Professional in 1993-1995	15.34	16.34	0.94	0.35
Poverty Rate in 1993-1995	-28.81	39.79	-0.72	0.47
Census Population (Thousands) in 1993-1995	0.00	0.00	-1.49	0.14
Percent Urban in 1993-1995	28.71	8.31	3.45	0.00
Change in Percent Male 1993-1995 to 2018-2019	54.77	183.24	0.30	0.77
Change in Percent Under 15 1993-1995 to 2018-2019	-146.87	83.85	-1.75	0.08
Change in Percent 15 to 29 1993-1995 to 2018-2019	-114.63	66.27	-1.73	0.08
Change in Percent 30 to 44 1993-1995 to 2018-2019	-238.75	66.51	-3.59	0.00
Change in Percent 45 to 64 1993-1995 to 2018-2019	-36.79	106.85	-0.34	0.73
Change in Percent White 1993-1995 to 2018-2019	45.26	22.26	2.03	0.04
Change in Percent Black 1993-1995 to 2018-2019	25.13	27.73	0.91	0.37
Change in Percent Hispanic 1993-1995 to 2018-2019	13.35	21.89	0.61	0.54
Change in Percent Less High School 1993-1995 to 2018-2019	-250.88	62.99	-3.98	0.00
Change in Percent High School 1993-1995 to 2018-2019	-36.62	36.11	-1.01	0.31
Change in Percent Some College 1993-1995 to 2018-2019	-174.19	55.00	-3.17	0.00
Change in Employment Ratio 1993-1995 to 2018-2019	71.15	24.16	2.94	0.00
Change in Percent Unemployed 1993-1995 to 2018-2019	288.79	101.88	2.83	0.00
Change in Median Household Income (Thousands) 1993-1995 to 2018-2019	-0.23	0.16	-1.40	0.16
Change in Percent Ag/M/Const/Util 1993-1995 to 2018-2019	28.12	25.84	1.09	0.28
Change in Percent Manufacturing 1993-1995 to 2018-2019	-44.47	20.73	-2.14	0.03
Change in Percent Retail/Transportation 1993-1995 to 2018-2019	-52.75	31.80	-1.66	0.10
Change in Percent Professional 1993-1995 to 2018-2019	3.97	20.23	0.20	0.84
Change in Poverty Rate 1993-1995 to 2018-2019	78.52	46.23	1.70	0.09
Change in Census Population (Thousands) 1993-1995 to 2018-2019	0.00	0.00	-0.52	0.61
Change in Percent Urban 1993-1995 to 2018-2019	26.37	13.37	1.97	0.05
Constant	-70.49	73.31	-0.96	0.34

Source: NCHS Mortality Data; U.S. Census Data; ARCOS Data.

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1. Comparison of regression results based on state data (Appendix Exhibit 9.6 / Model 1A) and large county data (Appendix Exhibit 9.6 / Model 1B) indicates that the impact of shipments on the growth of opioid mortality estimated using state data is materially larger than that estimated using county data.

Appendix Exhibit 9.6

Regression Estimates of the Relationship Between Shipments and Opioid Mortality Through 2010

Model	Data Sample	Mortality Type	Base Period	Post Period	Coefficient on Shipments				Implied Impact of Increase in Shipments on Post-Period Mortality Rate		
					Beta	Std. Err.	T-Stat.	P-Value	Implied		
									Actual Mortality Rate	But-For Mortality Rate	Percent Elevation
1A	States	Any Opioid	1993-1995	2009-2010	8.57	1.48	5.80	0.00	11.86	3.26	263.3%
1B	Large Counties	Any Opioid	1993-1995	2009-2010	4.04	0.48	8.46	0.00	11.63	7.55	54.0%
2A	States	Rx Opioids	1999-2000	2009-2010	5.27	1.18	4.46	0.00	7.99	2.71	195.0%
2B	Large Counties	Rx Opioids	1999-2000	2009-2010	2.37	0.37	6.41	0.00	6.92	4.52	52.9%
3A	States	Illicit Opioids	1999-2000	2009-2010	0.30	0.35	0.85	0.40	1.58	1.28	23.4%
3B	Large Counties	Illicit Opioids	1999-2000	2009-2010	0.50	0.31	1.61	0.11	2.49	1.99	25.6%

Notes:

Control variables for state regressions: Shipments per capita per day (average 1997-2010); base period non-mortality harm rate; change in percent of population white; change in median household income; change in percent less than high school; change in prime male employment to population; percentage change in total population.

Control variables for large county regressions: Shipments per capita per day (average 1997-2010); age <15, 15-29, 30-44, 45-64; percent male; percent white, black, hispanic; percent less than high school, high school only, some college; employment to population ratio; unemployment rate; median household income; percent employment in agriculture/construction/utilities, manufacturing, retail/transportation, professional services; poverty rate; percent urban; population; and changes in all variables.

Robust standard errors

But-For mortality based on assumption that shipments remain at 1997 levels.

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Appendix Exhibit 9.7

Regression Estimates of the Relationship Between Shipments and Opioid Mortality Through 2019

Model	Data Sample	Mortality Type	Base Period	Post Period	Coefficient on Shipments				Implied Impact of Increase in Shipments on Post-Period Mortality Rate		
					Beta	Std. Err.	T-Stat.	P-Value	Implied		
									Actual Mortality Rate	But-For Mortality Rate	Percent Elevation
4A	States	Illicit Opioids	2009-2010	2018-2019	10.69	3.71	2.88	0.01	14.48	3.76	284.6%
4B	Large Counties	Illicit Opioids	2009-2010	2018-2019	4.01	1.29	3.11	0.00	17.80	13.75	29.4%
5A	States	Any Opioid	1993-1995	2018-2019	13.16	4.37	3.01	0.00	19.90	6.70	197.0%
5B	Large Counties	Any Opioid	1993-1995	2018-2019	7.47	1.29	5.77	0.00	22.91	15.38	49.0%

Notes:

Control variables for state regressions: Shipments per capita per day (average 1997-2010); base period non-mortality harm rate; change in percent of population white; change in median household income; change in percent less than high school; change in prime male employment to population; percentage change in total population.

Control variables for large county regressions: Shipments per capita per day (average 1997-2010); age <15, 15-29, 30-44, 45-64; percent male; percent white, black, hispanic; percent less than high school, high school only, some college; employment to population ratio; unemployment rate; median household income; percent employment in agriculture/construction/utilities, manufacturing, retail/transportation, professional services; poverty rate; percent urban; population; and changes in all variables.

Robust standard errors

But-For mortality based on assumption that shipments remain at 1997 levels.

2. Specifically, an increase in per capita shipments of 1 MME per day is estimated to result in an increase of opioid mortality between 1993-95 and 2009-10 of 4.04 per 100,000 in the large county analysis and an increase of 8.57 per 100,000 in the state analysis. This difference appears to be due in part to the fact that the relationship between opioid shipments and mortality is larger in smaller counties than in the counties in the large county sample. The counties in the regression account for 70 percent of the U.S. population, compared to 100 percent coverage for the state-level analysis.

3. Because the county-level regression analyses include a considerably larger number of observations, they include a broader set of economic and demographic factors than the state versions. In addition, the county-level regressions include each of the economic and

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demographic factors in two ways: (i) the average value for the factor in the base period, and (ii) the change in the factor between the base and post periods.

4. To investigate the differences between the results based on state and county data, I combined the state and county data to construct two observations per state: one that measures total mortality and per capita shipments for the counties within the state that are included in the large county sample; the other for the remaining counties in the state.

Appendix Exhibit 9.8 graphically summarizes the results of this analysis and compares the increase in opioid mortality between 1993-95 and 2009-10 in four groups of states, classified based on average per capita shipments in the state between 1997 and 2010.

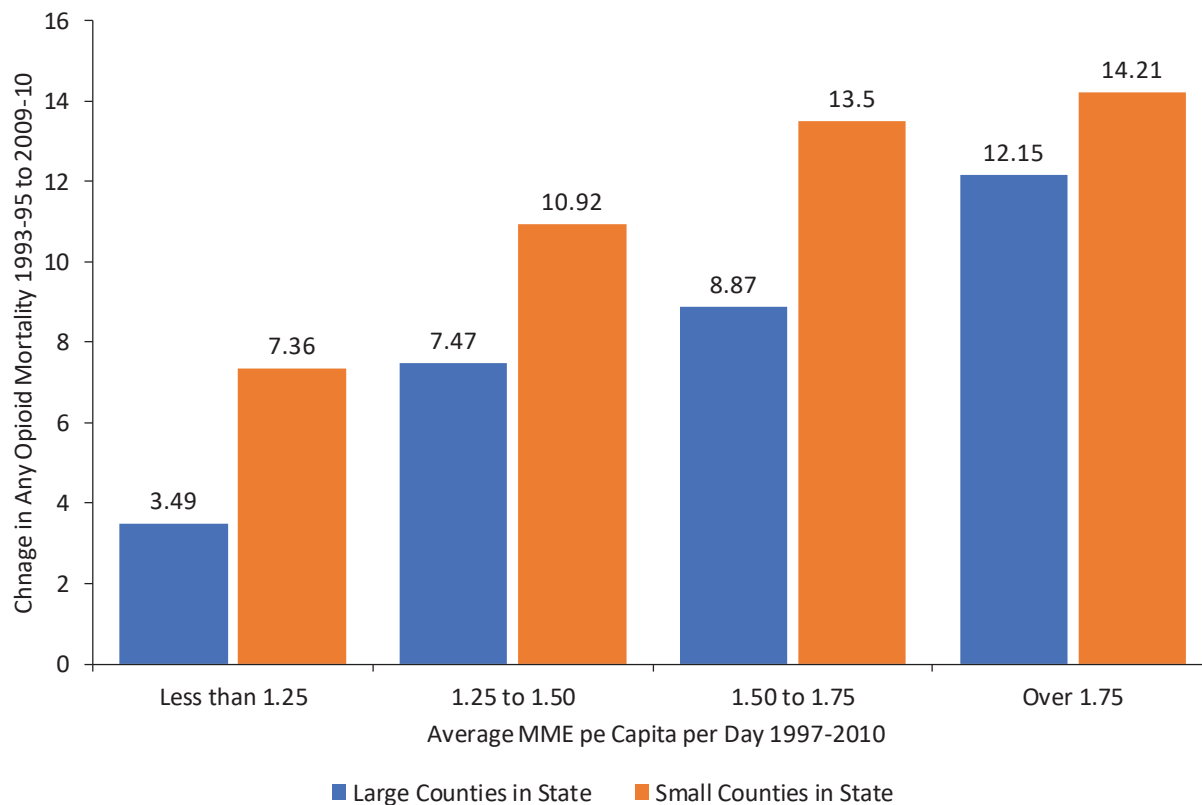
5. As the figure indicates, for each of the four groups of states classified based on shipments received, the increase in opioid mortality between 1993-95 and 2009-10 was larger in the state's small counties than in the state's large counties. On average across states in 1993-95, opioid mortality in large counties (3.2 per 100,000) was higher than in small counties (1.5 per 100,000). However, this gap was nearly eliminated by 2009-10, when mortality was 11.9 per 100,000 in large counties compared to 11.8 per 100,000 in small counties.

6. Economic theory does not indicate whether the relationship between opioid shipments and mortality should be greater in larger or small counties. The prediction depends on how many of the prescriptions in the area are appropriate, how easy it is to divert pills from intended to unintended users, differences in treatment availability, and other factors. Nevertheless, the results of this analysis indicate that a given increase in shipments in small counties results in a larger increase in mortality than the same increase in shipments in large counties.

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Appendix Exhibit 9.8

**Increases in Opioid Mortality between 1993-95 and 2009-10 in Large and Small Counties
Within States Classified by Shipments Between 1997-2010**



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Appendix 10: Overview of Economic and Epidemiological Studies of the Sources of the Illicit Opioid Crisis

1. A wide variety of economic and epidemiological researchers also conclude that a chain of events stemming from the increase in shipments of prescription opioids since the 1990s followed by a variety of policy responses to the prescription opioid crisis led to dramatic increase in harms from illicit opioids.

Economic Analyses

2. Alpert, Powell and Pacula (2018) conclude that “OxyContin reformulation significantly reduced OxyContin misuse, but also led to a large increase in heroin deaths. States with the highest initial rates of OxyContin misuse experienced the largest increases in heroin deaths. Event study results show that this differential increase in heroin deaths began precisely in the year following reformulation.”²⁰⁵

3. Evans, Lieber and Powell (2019) note that “[w]hen we combine heroin and opioid deaths together, we find no evidence that total heroin and opioid deaths fell at all after the reformulation—there appears to have been one-for-one substitution of heroin deaths for opioid deaths. Thus, it appears that the purpose for the abuse-deterrent reformulation of OxyContin was completely undone by changes in consumer behavior.”²⁰⁶

4. Alpert, Evans, Lieber, and Powell (2019) show that a state's exposure to distribution of OxyContin in the years after its introduction explains a large share of opioid-related mortality in the decades that follow. The authors show that Purdue Pharmaceutical focused its efforts to market the newly launched OxyContin in states that did not use so-called

²⁰⁵ Alpert, Abby, David Powell and Rosalie Liccardo Pacula. “Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids.” *American Economic Journal: Economic Policy* 10, no. 4 (2018): 1-35, p. 4.

²⁰⁶ Evans, William N., Ethan Lieber, Patrick Power. “How the Reformulation of Oxycontin Ignited the Heroin Epidemic.” *Review of Economics and Statistics* 101 no. 1 (2019): 1-15 (“Evans et al. (2019)”), at p. 2.

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"triplicate" programs. These programs require physicians to use state-issued prescription forms for Schedule II controlled substances and thus increase the burden on physicians in writing opioid prescriptions.²⁰⁷ The authors find that states with triplicate programs have substantially lower overdose rates (including those from prescription and illicit opioids) from 1996 through 2017 and a state's exposure to OxyContin explains a large share of variation in opioid mortality across states. They conclude: "[o]verall, our estimates imply that non-triplicate states would have had an average of 36% fewer drug overdose deaths and 44% fewer opioid overdose deaths in 1996-2017 if they had been triplicate states."²⁰⁸

5. Powell and Pacula (2020) show that states with greater exposure to OxyContin misuse experienced larger increases in mortality due to heroin, fentanyl, and cocaine through 2017. They conclude that these increases are causally related to the reformulation of OxyContin and the subsequent transition from prescription to illicit opioid abuse:²⁰⁹

[W]e uncover evidence that [OxyContin] reformulation led to the increase in total drug fatal overdoses, driving it to unprecedented levels; through the expansion of illicit drug markets.

6. Powell and Pacula (2020) also directly connect the rise of fentanyl mortality to restrictions of prescription opioids, noting that "[a]s the market evolved, we observe a delayed but even more dramatic rise in synthetic opioid deaths in states more exposed to reformulation. This link to reformulation suggests that the rise in illicit fentanyl was driven by demand considerations existing years prior to the entry of fentanyl. Synthetic opioids

²⁰⁷ These forms included three separate copies of the prescription: one retained by the physician, one maintained by the pharmacy, and one reported to the state drug monitoring agency.

²⁰⁸ Alpert, Abby E., William N. Evans, Ethan M.J. Lieber, and David Powell, "Origins of the Opioid Crisis and Its Enduring Impacts," NBER Working Paper 26500, November 2019 at p. 4.

²⁰⁹ Powell, David and Rosalie Liccario Pacula. "The Evolving Consequences of Oxycontin Reformulation on Drug Overdoses." NBER Working Paper 26988, April 2020, Revised in August 2020 ("Powell and Pacula (2020)"), at p. 3.

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disproportionately affected states that had higher rates of OxyContin misuse, even conditional on pain reliever misuse more generally.²¹⁰

7. Maclean et al. (2020) survey this growing economic literature on the causal sources of the opioid crisis. They conclude:

To summarize, the opioid crisis can be viewed through an economic lens as resulting from an interaction between supply-side and demand-side factors, and feedback between the two. At the most fundamental level, supply-side factors related to the increased production and marketing of opioids, combined with changes in prescribing patterns and policies (e.g. the Joint Commission listing pain as the fifth vital sign) were the proximate cause. These factors explain why the crisis began, fairly suddenly, in the late 1990s, after the approval of OxyContin and pharmaceutical industry efforts to normalize the prescribing of opioids. Conversely, demand-side factors such as skills-based technological change and import competition are unable to account for the timing of the increase in opioid prescriptions and the resulting adverse consequences.²¹¹

Epidemiological Studies

8. Several epidemiological studies provide supplemental evidence that prescription opioids were the predominant gateway to the growth of heroin use and the illicit opioid crisis after 2010. While the epidemiological evidence is not uniform – as one would expect, given that many of the studies rely on small samples from particular areas in the country - many studies have concluded that initiation of illicit opioid use after 2010 is a consequence of prior use of prescription opioids. A more comprehensive review of this literature is presented by other experts.

9. Jones et al. (2013), compares NSDUH Survey Data from 2002-04 and 2008-10 and find that rates of heroin use among nonmedical users of opioid pain relievers nearly

²¹⁰ Powell and Pacula (2020),p. 24.

²¹¹ Maclean et al. (2020), pp. 11-12.

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doubled between 2002-04 and 2008-10, from 1.8 percent to 3.4 percent.²¹² However, no increase in heroin use was observed among respondents who did not report nonmedical use of prescription opioids in the prior year.

10. Muhuri et al. (2013) also analyze NSDUH data and find “a strong association between prior nonmedical use of pain relievers and the subsequent past year initiation of heroin use.”²¹³ They find that the heroin incidence rate was 19 times higher among those who reported prior nonmedical prescription pain reliever (NMPPR) use than among those who did not report NMPPR use.²¹⁴

11. Cicero, et al. (2014) evaluate survey data of patients in public and private drug treatment centers who reported heroin as their primary drug of abuse.²¹⁵ The survey was conducted between 2010 Q3 and 2013 Q3 and covered a population of individuals who had received a primary diagnosis of heroin use/dependence. The survey establishes that among respondents who began using opioids in the 2000s, 75 percent initiated opioid use with prescription opioids, with this share declining to roughly 65 percent for those that initiated opioid abuse in 2010-13.²¹⁶

12. Additional small-sample epidemiological studies confirm these findings: Mateu-Gelabert, et al. (2015) interviewed 46 adults between the ages of 18 and 32 in New York City in

²¹² Jones, Christopher M. “Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers—United States, 2002–2004 and 2008–2010.” *Drug and Alcohol Dependence* 132 (2013): 95-100. (“Jones (2013)”). Table 1.

²¹³ Muhuri, Pradip K., Joseph C. Gfroerer, and M. Christine Davies. “Associations of nonmedical pain reliever use and initiation of heroin use in the United States.” *CBHSQ Data Review* 2013 (August) (“Muhuri et al (2013)”), at p. 14

²¹⁴ Muhuri et al (2013), at p. 9.

²¹⁵ Cicero, Theodore J., Matthew S. Ellis, Hilary L. Surratt, Steven P. Kurtz. “The Changing Face of Heroin Use in the United States, A Retrospective Analysis of the Past 50 Years.” *JAMA Psychiatry* 71(7) (2014): 821-826 (“Cicero et al. (2014)”).

²¹⁶ Cicero et al (2014), at pp. 822-823 and Figure 1.

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2012-13 who had reported “lifetime use of [prescription opioids] for nonmedical reasons.”²¹⁷

The authors find that 32 out of the 46 individuals (70 percent) eventually began using heroin, which then typically became the primary drug of choice displacing prescription opioids.²¹⁸

13. Cicero and Ellis (2015) study the impact of abuse deterrent formulations (ADFs) of prescription opioids on heroin use among patients in public and private treatment centers.²¹⁹ The authors find that use of heroin in the past month among respondents steadily increased during the four years after ADF introduction (from approximately 25 percent to 50 percent of respondents).²²⁰ The authors interviewed 153 individuals who had indicated prior abuse of OxyContin and among these, 51 indicated the introduction of the ADF led them to shift drug choices. Among those that reported what drug they switched to, roughly two-thirds switched to heroin.²²¹

²¹⁷ Mateu-Gelabert, Pedro, Honoria Guarino, Lauren Jessell, and Anastasia Teper. “Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City.” *Journal of Substance Abuse Treatment* 48 (2015): 13-20 (“Mateu-Gelabert et al (2015)”), p. 14.

²¹⁸ Mateu-Gelabert et al (2015), p. 14.

²¹⁹ Cicero, Theodore J. and Matthew S. Ellis. “Abuse-deterrent formulations and the prescription opioid abuse epidemic in the United States: Lessons learned from OxyContin.” *JAMA Psychiatry* 72 (2015): 424-430. (“Cicero et al (2015)”).

²²⁰ Cicero et al (2015), Figure 1.

²²¹ Cicero et al (2015), pp. 426-427.

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Appendix 11: Regression Estimation of the Relationship Between Shipments and Other Harms

Appendix Exhibit 11.1 Relationship between Per Capita Shipments and Change in Opioid Use Disorder Rate from 2002-2003 to 2018-2019

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.40

Variable	Coef.	Std. Err	t	P> t
Change in Opioid Use Disorder Rate				
Avg. Shipments per Capita per Day (1997-2010)	416.34	117.58	3.54	0.00
Opioid Use Disorder Rate in 2002-2003	-0.74	0.14	-5.35	0.00
Change in Median Household Income (Thousands) 2002-2003 to 2018-2019	15.49	19.31	0.80	0.43
Change in Prime Male Employment to Population 2002-2003 to 2018-2019	1228.55	2257.67	0.54	0.59
Change in Percent White 2002-2003 to 2018-2019	898.96	2675.65	0.34	0.74
Change in Percent Less High School 2002-2003 to 2018-2019	1370.70	3303.54	0.41	0.68
Change in Census Population (Thousands) 2002-2003 to 2018-2019	-283.13	432.91	-0.65	0.52
Constant	66.07	245.59	0.27	0.79

Source: NSDUH; U.S. Census Data; ARCOS Data.

Appendix Exhibit 11.2 Relationship between Per Capita Shipments and Change in Heroin Use Disorder Rate from 2002-2003 to 2018-2019

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.08

Variable	Coef.	Std. Err	t	P> t
Change in Heroin Use Disorder Rate				
Avg. Shipments per Capita per Day (1997-2010)	163.57	60.96	2.68	0.01
Heroin Use Disorder Rate in 2002-2003	-0.45	0.28	-1.57	0.12
Change in Median Household Income (Thousands) 2002-2003 to 2018-2019	1.80	7.00	0.26	0.80
Change in Prime Male Employment to Population 2002-2003 to 2018-2019	207.16	1278.94	0.16	0.87
Change in Percent White 2002-2003 to 2018-2019	-122.26	1492.54	-0.08	0.94
Change in Percent Less High School 2002-2003 to 2018-2019	2556.76	1737.48	1.47	0.15
Change in Census Population (Thousands) 2002-2003 to 2018-2019	-282.11	157.34	-1.79	0.08
Constant	67.23	136.48	0.49	0.62

Source: NSDUH; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 11.3
Relationship between Per Capita Shipments and NAS Hospitalization Rate from
2008-2009 to 2017-2018

States

Ordinary Least Squares Regression

Number of obs = 42

Robust Standard Errors

Adjusted R-squared = 0.49

Variable	Coef.	Std. Err	t	P> t
Change in NAS Hospitalization Rate				
Avg. Shipments per Capita per Day (1997-2010)	7.52	3.02	2.49	0.02
NAS Hospitalization Rate in 2008-2009	0.51	0.25	2.05	0.05
Change in Median Household Income (Thousands) 2008-2009 to 2017-2018	0.57	0.48	1.19	0.24
Change in Prime Male Employment to Population 2008-2009 to 2017-2018	-53.95	51.86	-1.04	0.31
Change in Percent White 2008-2009 to 2017-2018	31.09	68.68	0.45	0.65
Change in Percent Less High School 2008-2009 to 2017-2018	-233.15	110.97	-2.10	0.04
Change in Census Population (Thousands) 2008-2009 to 2017-2018	-31.31	18.80	-1.67	0.10
Constant	-10.53	5.17	-2.04	0.05

Source: HCUP; U.S. Census Data; ARCOS Data.

Appendix Exhibit 11.4
Relationship between Per Capita Shipments and Emergency Department Visit Rate from
2006-2007 to 2017-2018

States

Ordinary Least Squares Regression

Number of obs = 24

Robust Standard Errors

Adjusted R-squared = 0.55

Variable	Coef.	Std. Err	t	P> t
Change in Emergency Department Visit Rate				
Avg. Shipments per Capita per Day (1997-2010)	74.49	78.79	0.95	0.36
Emergency Department Visit Rate in 2006-2007	0.84	0.32	2.59	0.02
Change in Median Household Income (Thousands) 2006-2007 to 2017-2018	-5.25	10.08	-0.52	0.61
Change in Prime Male Employment to Population 2006-2007 to 2017-2018	517.95	1442.90	0.36	0.72
Change in Percent White 2006-2007 to 2017-2018	-3119.84	1867.38	-1.67	0.11
Change in Percent Less High School 2006-2007 to 2017-2018	-2401.92	1292.36	-1.86	0.08
Change in Census Population (Thousands) 2006-2007 to 2017-2018	-406.17	343.03	-1.18	0.25
Constant	-120.99	131.60	-0.92	0.37

Source: HCUP; U.S. Census Data; ARCOS Data.

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Appendix Exhibit 11.5
Relationship between Per Capita Shipments and Inpatient Stay Rate from
2006-2007 to 2017-2018

States

Ordinary Least Squares Regression

Number of obs = 38

Robust Standard Errors

Adjusted R-squared = 0.32

Variable	Coef.	Std. Err	t	P> t
Change in Inpatient Stay Rate				
Avg. Shipments per Capita per Day (1997-2010)	134.01	30.49	4.40	0.00
Inpatient Stay Rate in 2006-2007	-0.18	0.16	-1.12	0.27
Change in Median Household Income (Thousands) 2006-2007 to 2017-2018	7.75	5.63	1.38	0.18
Change in Prime Male Employment to Population 2006-2007 to 2017-2018	-221.59	609.60	-0.36	0.72
Change in Percent White 2006-2007 to 2017-2018	-1641.76	1013.09	-1.62	0.12
Change in Percent Less High School 2006-2007 to 2017-2018	-1197.53	861.77	-1.39	0.17
Change in Census Population (Thousands) 2006-2007 to 2017-2018	-311.96	182.54	-1.71	0.10
Constant	-88.24	49.83	-1.77	0.09

Source: HCUP; U.S. Census Data; ARCOS Data.

Appendix Exhibit 11.6
Relationship between Per Capita Shipments and Rate of Children in Foster Care from
2010-2011 to 2018-2019

States

Ordinary Least Squares Regression

Number of obs = 50

Robust Standard Errors

Adjusted R-squared = 0.05

Variable	Coef.	Std. Err	t	P> t
Change in Rate of Children in Foster Care				
Avg. Shipments per Capita per Day (1997-2010)	161.17	98.41	1.64	0.11
Rate of Children in Foster Care in 2010-2011	0.16	0.25	0.64	0.53
Change in Median Household Income (Thousands) 2010-2011 to 2018-2019	-5.80	15.81	-0.37	0.72
Change in Prime Male Employment to Population 2010-2011 to 2018-2019	-1673.60	1187.61	-1.41	0.17
Change in Percent White 2010-2011 to 2018-2019	4353.56	3974.45	1.10	0.28
Change in Percent Less High School 2010-2011 to 2018-2019	-1331.10	4131.28	-0.32	0.75
Change in Census Population (Thousands) 2010-2011 to 2018-2019	-673.27	656.29	-1.03	0.31
Constant	-35.52	190.63	-0.19	0.85

Source: AFCARS; U.S. Census Data; ARCOS Data.

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Appendix 12: Impact of Defendants on Total Opioid Mortality

Appendix Exhibit 12.1

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019

Scenario 1: Based on McCann Dispenser Analysis with Non-Recurrent Flags

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (2006-2010)	a	59%	48%
Flagged Percent of Defendants' MME (2006-2010)	b	37%	39%
Defendants' Flagged MMEs as Percent of Total	$c=a*b$	22%	19%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	d	12.68	18.75
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	e	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	$f=d-e$	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	$g=f*c$	0.97	1.17
Percent of Mortality Rate in 2009-2010 Attributable to Defendants	$h=g/d$	8%	6%
County Adult Population in 2009-2010	i	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	$j=g*(i/100,000)$	1.8	2.0
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	k	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	l	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	$m=k-l$	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	$n=m*c$	5.73	6.83
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	$o=f+m$	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	$p=g+n$	6.71	8.00
Percent of 2018-19 Mortality Rate Attributable to Defendants	$q=p/k$	20%	16%
County Adult Population in 2018-2019	r	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	$s=p*(r/100,000)$	12.9	13.2

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section X.C and Appendix 12.
Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

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Appendix Exhibit 12.2

Impact of Defendants on Annual Total Opioid Mortality By Year
Scenario 1: Based on McCann Dispenser Analysis with Non-Recurrent Flags

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	1%	0.01	0.0	1.95	0%	0.01	0.0
1997	3.01	1%	0.03	0.1	0.17	1%	0.00	0.0
1998	1.97	2%	0.03	0.1	4.13	1%	0.06	0.1
1999	3.85	2%	0.08	0.2	4.70	2%	0.08	0.2
2000	3.84	3%	0.11	0.2	4.62	2%	0.10	0.2
2001	2.19	3%	0.07	0.1	5.87	3%	0.16	0.3
2002	5.47	4%	0.21	0.4	10.68	3%	0.33	0.6
2003	1.09	4%	0.05	0.1	7.68	4%	0.27	0.5
2004	6.52	5%	0.32	0.6	17.52	4%	0.71	1.3
2005	8.13	5%	0.45	0.8	13.25	4%	0.59	1.0
2006	9.70	6%	0.58	1.1	17.22	5%	0.85	1.5
2007	12.55	7%	0.82	1.5	29.30	5%	1.57	2.7
2008	11.68	7%	0.83	1.6	19.46	6%	1.13	2.0
Avg. 2009-2010	12.68	8%	0.97	1.8	18.75	6%	1.17	2.0
2011	21.96	9%	2.01	3.8	29.51	7%	2.20	3.8
2012	22.17	11%	2.36	4.5	18.09	9%	1.57	2.7
2013	20.49	12%	2.49	4.7	20.62	10%	2.03	3.5
2014	26.11	14%	3.57	6.8	30.75	11%	3.40	5.8
2015	25.65	15%	3.89	7.4	50.64	12%	6.21	10.5
2016	47.70	17%	7.95	15.2	60.86	13%	8.20	13.8
2017	45.25	18%	8.22	15.8	70.64	15%	10.37	17.3
Avg. 2018-2019	34.12	20%	6.71	12.9	50.39	16%	8.00	13.2
Total Deaths Attributable to Defendants (1996-2019)				94.5	98.1			

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section X.C and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

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Appendix Exhibit 12.3
Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019
Scenario 3: Based on McCann Distributor Analysis

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (2006-2010)	<i>a</i>	36%	17%
Flagged Percent of Defendants' MME (2006-2010)	<i>b</i>	69%	69%
Defendants' Flagged MMEs as Percent of Total	<i>c=a*b</i>	25%	11%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	<i>d</i>	12.68	18.75
Beta on Shipments from Model 1		4.04	4.04
Actual Shipments 1997-2010		1.10	1.55
Impact of Shipments as of 2009-2010		4.46	6.25
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	<i>e</i>	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	<i>f=d-e</i>	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	<i>g=f*c</i>	1.11	0.71
Percent of Mortality Rate in 2009-2010 Attributable to Defendants	<i>h=g/d</i>	9%	4%
County Adult Population in 2009-2010	<i>i</i>	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	<i>j=g*(i/100,000)</i>	2.1	1.2
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	<i>k</i>	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	<i>l</i>	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	<i>m=k-l</i>	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	<i>n=m*c</i>	6.56	4.14
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	<i>o=f+m</i>	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	<i>p=g+n</i>	7.67	4.85
Percent of 2018-19 Mortality Rate Attributable to Defendants	<i>q=p/k</i>	22%	10%
County Adult Population in 2018-2019	<i>r</i>	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	<i>s=p*(r/100,000)</i>	14.8	8.0

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section VII.A.
Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

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Appendix Exhibit 12.4

Impact of Defendants on Annual Total Opioid Mortality By Year
Scenario 3: Based on McCann Distributor Analysis

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	1%	0.02	0.0	1.95	0%	0.01	0.0
1997	3.01	1%	0.04	0.1	0.17	1%	0.00	0.0
1998	1.97	2%	0.04	0.1	4.13	1%	0.03	0.1
1999	3.85	3%	0.10	0.2	4.70	1%	0.05	0.1
2000	3.84	3%	0.12	0.2	4.62	1%	0.06	0.1
2001	2.19	4%	0.08	0.2	5.87	2%	0.10	0.2
2002	5.47	4%	0.24	0.4	10.68	2%	0.20	0.4
2003	1.09	5%	0.05	0.1	7.68	2%	0.17	0.3
2004	6.52	6%	0.37	0.7	17.52	2%	0.43	0.8
2005	8.13	6%	0.51	0.9	13.25	3%	0.36	0.6
2006	9.70	7%	0.67	1.2	17.22	3%	0.51	0.9
2007	12.55	8%	0.94	1.8	29.30	3%	0.95	1.7
2008	11.68	8%	0.95	1.8	19.46	4%	0.69	1.2
Avg. 2009-2010	12.68	9%	1.11	2.1	18.75	4%	0.71	1.2
2011	21.96	10%	2.30	4.4	29.51	5%	1.34	2.3
2012	22.17	12%	2.71	5.1	18.09	5%	0.95	1.6
2013	20.49	14%	2.85	5.4	20.62	6%	1.23	2.1
2014	26.11	16%	4.08	7.8	30.75	7%	2.06	3.5
2015	25.65	17%	4.45	8.5	50.64	7%	3.77	6.4
2016	47.70	19%	9.09	17.4	60.86	8%	4.97	8.3
2017	45.25	21%	9.40	18.1	70.64	9%	6.28	10.5
Avg. 2018-2019	34.12	22%	7.67	14.8	50.39	10%	4.85	8.0
Total Deaths Attributable to Defendants (1996-2019)				108.1	59.4			

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section VII.A and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

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Appendix 13: Impact of Defendants on Total Opioid Mortality – Alternative Treatment of 1997-2005 Shipments

Appendix Exhibit 13.1 Impact of Defendants on Annual Total Opioid Mortality Total Number of Deaths Attributable to Defendants, 1996-2019 Based on 50% of 2006-2010 Average for 1997-2005

Scenario	Approach	County	
		Lake County	Trumbull County
1	Dispenser Analysis, Non-Recurrent, 2006-2010 [1]	74.0	76.6
2	Dispenser Analysis, Recurrent, 2006-2010 [2]	188.2	188.5
3	Distributor Analysis, 2006-2010 [3]	84.6	46.4

Notes:

[1] Flagged MMEs based on 2006-2010 MMEs per McCann Section X.C and Appendix 12.

[2] Flagged MMEs based on 2006-2010 MMEs per McCann Section X.B and Appendix 12.

[3] Flagged MMEs based on 2006-2010 MMEs per McCann Section VII.A.

For calculation, flagged MME percentages for 1997-2005 set to 50% of 2006-2010 average.

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Appendix Exhibit 13.2

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019
Scenario 1: Based on McCann Dispenser Analysis with Non-Recurrent Flags
Based on 50% of 2006-2010 Average for 1997-2005

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (1997-2010)	<i>a</i>	59%	48%
Flagged Percent of Defendants' MME (1997-2010)	<i>b</i>	29%	30%
Defendants' Flagged MMEs as Percent of Total	$c=a*b$	17%	15%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	<i>d</i>	12.68	18.75
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	<i>e</i>	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	$f=d-e$	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	$g=f*c$	0.76	0.92
Percent of Mortality Rate in 2009-2010 Attributable to	$h=g/d$	6%	5%
County Adult Population in 2009-2010	<i>i</i>	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	$j=g*(i/100,000)$	1.4	1.6
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	<i>k</i>	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	<i>l</i>	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	$m=k-l$	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	$n=m*c$	4.49	5.33
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	$o=f+m$	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	$p=g+n$	5.25	6.25
Percent of 2018-19 Mortality Rate Attributable to Defendants	$q=p/k$	15%	12%
County Adult Population in 2018-2019	<i>r</i>	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	$s=p*(r/100,000)$	10.1	10.3

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section X.C and Appendix 12.
Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).
For calculation, flagged MME percentages for 1997-2005 set to 50% of 2006-2010 average.

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Appendix Exhibit 13.3

Impact of Defendants on Annual Total Opioid Mortality By Year
Scenario 1: Based on McCann Dispenser Analysis with Non-Recurrent Flags
Based on 50% of 2006-2010 Average for 1997-2005

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	0%	0.01	0.0	1.95	0%	0.01	0.0
1997	3.01	1%	0.03	0.0	0.17	1%	0.00	0.0
1998	1.97	1%	0.03	0.0	4.13	1%	0.04	0.1
1999	3.85	2%	0.07	0.1	4.70	1%	0.07	0.1
2000	3.84	2%	0.08	0.2	4.62	2%	0.08	0.1
2001	2.19	3%	0.06	0.1	5.87	2%	0.12	0.2
2002	5.47	3%	0.16	0.3	10.68	2%	0.26	0.5
2003	1.09	3%	0.04	0.1	7.68	3%	0.21	0.4
2004	6.52	4%	0.25	0.5	17.52	3%	0.55	1.0
2005	8.13	4%	0.35	0.6	13.25	3%	0.46	0.8
2006	9.70	5%	0.46	0.8	17.22	4%	0.66	1.2
2007	12.55	5%	0.65	1.2	29.30	4%	1.23	2.1
2008	11.68	6%	0.65	1.2	19.46	5%	0.88	1.5
Avg. 2009-2010	12.68	6%	0.76	1.4	18.75	5%	0.92	1.6
2011	21.96	7%	1.58	3.0	29.51	6%	1.72	3.0
2012	22.17	8%	1.85	3.5	18.09	7%	1.22	2.1
2013	20.49	10%	1.95	3.7	20.62	8%	1.59	2.7
2014	26.11	11%	2.79	5.3	30.75	9%	2.66	4.5
2015	25.65	12%	3.04	5.8	50.64	10%	4.85	8.2
2016	47.70	13%	6.22	11.9	60.86	11%	6.41	10.7
2017	45.25	14%	6.43	12.4	70.64	11%	8.10	13.5
Avg. 2018-2019	34.12	15%	5.25	10.1	50.39	12%	6.25	10.3
Total Deaths Attributable to Defendants (1996-2019)				74.0	76.6			

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section X.C and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

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Appendix Exhibit 13.4

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019
Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags
Based on 50% of 2006-2010 Average for 1997-2005

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (1997-2010)	a	59%	48%
Flagged Percent of Defendants' MME (1997-2010)	b	74%	75%
Defendants' Flagged MMEs as Percent of Total	$c=a*b$	43%	36%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	d	12.68	18.75
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	e	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	$f=d-e$	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	$g=f*c$	1.94	2.26
Percent of Mortality Rate in 2009-2010 Attributable to	$h=g/d$	15%	12%
County Adult Population in 2009-2010	i	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	$j=g*(i/100,000)$	3.6	3.9
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	k	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	l	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	$m=k-l$	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	$n=m*c$	11.42	13.13
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	$o=f+m$	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	$p=g+n$	13.35	15.38
Percent of 2018-19 Mortality Rate Attributable to Defendants	$q=p/k$	39%	31%
County Adult Population in 2018-2019	r	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	$s=p*(r/100,000)$	25.8	25.4

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section X.B and Appendix 12.
Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).
For calculation, flagged MME percentages for 1997-2005 set to 50% of 2006-2010 average.

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Appendix Exhibit 13.5

Impact of Defendants on Annual Total Opioid Mortality By Year
Scenario 2: Based on McCann Dispenser Analysis with Recurrent Flags
Based on 50% of 2006-2010 Average for 1997-2005

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	1%	0.03	0.0	1.95	1%	0.02	0.0
1997	3.01	2%	0.07	0.1	0.17	2%	0.00	0.0
1998	1.97	3%	0.06	0.1	4.13	3%	0.11	0.2
1999	3.85	4%	0.17	0.3	4.70	3%	0.16	0.3
2000	3.84	5%	0.21	0.4	4.62	4%	0.20	0.4
2001	2.19	7%	0.14	0.3	5.87	5%	0.30	0.5
2002	5.47	8%	0.42	0.8	10.68	6%	0.64	1.1
2003	1.09	9%	0.10	0.2	7.68	7%	0.53	0.9
2004	6.52	10%	0.64	1.2	17.52	8%	1.36	2.4
2005	8.13	11%	0.89	1.6	13.25	9%	1.14	2.0
2006	9.70	12%	1.16	2.2	17.22	9%	1.63	2.9
2007	12.55	13%	1.64	3.1	29.30	10%	3.02	5.3
2008	11.68	14%	1.66	3.1	19.46	11%	2.18	3.8
Avg. 2009-2010	12.68	15%	1.94	3.6	18.75	12%	2.26	3.9
2011	21.96	18%	4.01	7.6	29.51	14%	4.23	7.3
2012	22.17	21%	4.71	8.9	18.09	17%	3.01	5.2
2013	20.49	24%	4.96	9.4	20.62	19%	3.91	6.7
2014	26.11	27%	7.10	13.5	30.75	21%	6.55	11.1
2015	25.65	30%	7.74	14.8	50.64	24%	11.95	20.2
2016	47.70	33%	15.82	30.3	60.86	26%	15.77	26.5
2017	45.25	36%	16.36	31.5	70.64	28%	19.93	33.2
Avg. 2018-2019	34.12	39%	13.35	25.8	50.39	31%	15.38	25.4
Total Deaths Attributable to Defendants (1996-2019)				188.2	188.5			

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section X.B and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.

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Appendix Exhibit 13.6

Impact of Defendants on Annual Total Opioid Mortality in 2009-2010 and 2018-2019

Scenario 3: Based on McCann Distributor Analysis

Based on 50% of 2006-2010 Average for 1997-2005

		County	
		Lake County	Trumbull County
<u>Defendants' Flagged MMEs</u>			
Defendants' Percent of Total MMEs (1997-2010)	a	36%	17%
Flagged Percent of Defendants' MME (1997-2010)	b	54%	54%
Defendants' Flagged MMEs as Percent of Total	$c=a*b$	20%	9%
<u>Impact on Mortality through 2009-2010</u>			
Actual Opioid Mortality Rate in 2009-2010	d	12.68	18.75
Beta on Shipments from Model 1		4.04	4.04
Actual Shipments 1997-2010		1.10	1.55
Impact of Shipments as of 2009-2010		4.46	6.25
Predicted Mortality Rate in 2009-2010 (Direct Regression on Change from 1993-95 to 2009-10)	e	8.22	12.50
Mortality Rate in 2009-10 Attributable to All Shipments	$f=d-e$	4.46	6.25
Mortality Rate in 2009-10 Attributable to Defendants	$g=f*c$	0.87	0.56
Percent of Mortality Rate in 2009-2010 Attributable to Defendants	$h=g/d$	7%	3%
County Adult Population in 2009-2010	i	188,356	172,620
Annual Opioid-Related Deaths (2009-2010 Average) Attributable to Defendants	$j=g*(i/100,000)$	1.6	1.0
<u>Incremental Impact on Mortality through 2018-2019</u>			
Actual Opioid Mortality Rate 2018-2019	k	34.12	50.39
Predicted Mortality Rate in 2018-19 (Indirect Regression based on 2009-10 Predicted for 2018-19)	l	7.83	14.02
Incremental Mortality Rate in 2018-19 Attributable to All Shipments	$m=k-l$	26.28	36.37
Incremental Mortality Rate in 2018-19 Attributable to Defendants	$n=m*c$	5.13	3.23
<u>Total Impact on Mortality through 2018-2019</u>			
Total Mortality Rate in 2018-19 Attributable to All Shipments	$o=f+m$	30.74	42.63
Total Mortality Rate in 2018-19 Attributable to Defendants	$p=g+n$	6.01	3.79
Percent of 2018-19 Mortality Rate Attributable to Defendants	$q=p/k$	18%	8%
County Adult Population in 2018-2019	r	193,073	165,166
Annual Opioid-Related Deaths (2018-19 Average) Attributable to Defendants	$s=p*(r/100,000)$	11.6	6.3

Notes: Flagged MMEs based on 2006-2010 MMEs per McCann Section VII.A.

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

For calculation, flagged MME percentages for 1997-2005 set to 50% of 2006-2010 average.

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Appendix Exhibit 13.7

Impact of Defendants on Annual Total Opioid Mortality By Year

Scenario 3: Based on McCann Distributor Analysis

Based on 50% of 2006-2010 Average for 1997-2005

Period	Lake County				Trumbull County			
	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants	Actual Mortality Rate	Percent Attributable to Defendants	Mortality Rate Attributable to Defendants	Number of Deaths Attributable to Defendants
	<i>a</i>	<i>b</i>	<i>c=a*b</i>	<i>d=c*population /100,000</i>	<i>e</i>	<i>f</i>	<i>g=e*f</i>	<i>h=e*population /100,000</i>
Avg. 1993-1995	1.24	0%	0.00	0.0	0.81	0%	0.00	0.0
1996	2.40	0%	0.01	0.0	1.95	0%	0.00	0.0
1997	3.01	1%	0.03	0.1	0.17	0%	0.00	0.0
1998	1.97	1%	0.03	0.1	4.13	1%	0.03	0.0
1999	3.85	2%	0.08	0.1	4.70	1%	0.04	0.1
2000	3.84	2%	0.09	0.2	4.62	1%	0.05	0.1
2001	2.19	3%	0.06	0.1	5.87	1%	0.07	0.1
2002	5.47	3%	0.19	0.3	10.68	1%	0.16	0.3
2003	1.09	4%	0.04	0.1	7.68	2%	0.13	0.2
2004	6.52	4%	0.29	0.5	17.52	2%	0.33	0.6
2005	8.13	5%	0.40	0.7	13.25	2%	0.28	0.5
2006	9.70	5%	0.52	1.0	17.22	2%	0.40	0.7
2007	12.55	6%	0.74	1.4	29.30	3%	0.74	1.3
2008	11.68	6%	0.75	1.4	19.46	3%	0.54	0.9
Avg. 2009-2010	12.68	7%	0.87	1.6	18.75	3%	0.56	1.0
2011	21.96	8%	1.80	3.4	29.51	4%	1.04	1.8
2012	22.17	10%	2.12	4.0	18.09	4%	0.74	1.3
2013	20.49	11%	2.23	4.2	20.62	5%	0.96	1.6
2014	26.11	12%	3.20	6.1	30.75	5%	1.61	2.7
2015	25.65	14%	3.48	6.7	50.64	6%	2.94	5.0
2016	47.70	15%	7.12	13.6	60.86	6%	3.88	6.5
2017	45.25	16%	7.36	14.1	70.64	7%	4.91	8.2
Avg. 2018-2019	34.12	18%	6.01	11.6	50.39	8%	3.79	6.3
Total Deaths Attributable to Defendants (1996-2019)				84.6	46.4			

Notes:

Mortality rates based on any opioid overdose deaths per 100,000 adults (age 15+).

Mortality attributable to defendants in 2009-2010 and 2018-2019 based on McCann Section VII.A and regression analysis described above.

Mortality attributable to defendants in intervening years based on linear growth in attribution rate.